



THE  
AMERICAN JOURNAL

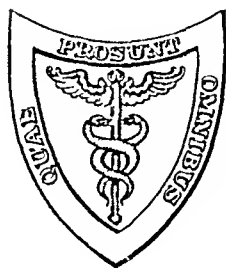
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MEDICAL SCIENCES

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ORIGINAL ARTICLES

THE INFLUENCE OF WAR UPON INFANT MORTALITY AND  
ITS MEANING.<sup>1</sup>

BY SAMUEL MCC. HAMILL, M.D.,

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COMMONWEALTH OF PENNSYLVANIA.

THE factors that determine the population of any country are:

1. The number of children born into it.
2. The number of people that die in it.
3. The number of people that go out of or come into it.

Therefore to prevent a decrease in population or to maintain an increase—the goal of every nation—it is necessary to have a high birth-rate and a low death-rate and to successfully encourage desirable immigration.

All of these problems have received serious consideration in the past.

The birth-rate has shown a tendency to decrease in nearly every country in recent years, and especially in those most highly civilized. France was the one whose future was most seriously threatened before this war.

Through increased governmental activity, and more especially through the establishment of many volunteer welfare agencies, the nations had been endeavoring to compensate for the lowered birth-rate by saving the lives of babies under one year of age—a period of life in which the death-rate was extraordinarily high and in which the diseases causing the death-rate were largely of the preventable

<sup>1</sup> Read before the Philadelphia Pediatric Society, November 13, 1917.



group. Much had been accomplished before the war in some countries, and yet in but few of them could it be said that more than a mere beginning had been made.

New Zealand was the one brilliant exception. In 1907 her infant death-rate was 80 per thousand living births. In 1913 it had been reduced to 38 per thousand living births, thus verifying the opinion that it is possible to save practically 50 per cent. of the babies that are dying today.

What have we been doing in this country to reduce infant mortality?

Our Federal, State, and Municipal Governments have not become sufficiently aroused to the importance of saving human life.

In 1917 the Federal Government made the munificent appropriation of \$296,250 for the work of its Children's Bureau.

In the same year it *increased* its appropriation for the battle against foot-and-mouth disease among cattle by \$2,500,000 and appropriated for the control of hog cholera the sum of \$360,000. These last two appropriations were very necessary. Foot-and-mouth disease and hog cholera should be wiped out. But is their elimination relatively so much more important than the control of the contagious diseases of childhood or the education of the people of the nation in the methods of preventing death and disease among infants and children?

Speaking of education reminds us of the anomalous position in which we find ourselves in respect to the relative amounts appropriated for the maintenance of the health of our people and the education of our children. Health is fundamental to all progress. What is the use of developing the minds of our children if they are not physically equal to the battle of life? And yet the Pennsylvania State Board of Health has recently reported that 71.5 per cent. of the children coming to the public schools carry one or more physical defects of such importance as to modify seriously their efficiency or to threaten interference with their later development.

The recent experiences of the United States Government in its attempt to raise an army to fight the unspeakable Hun have confirmed this experience by revealing the humiliating fact that the number of our young men *physically unfit* for military service is extremely large.

Physically unfit, and yet the city of New York, in 1917, appropriated \$41,430,447 for the *education of its children* and only \$3,326,041 for the *protection of the health of all its people*. Of this amount but \$650,625 was awarded to the Division of Child Hygiene. Out of this latter sum also is taken the salaries of all medical inspectors of the city—including school inspectors.

I mention New York because her health appropriation is relatively very large, and because, with this measly pittance, she has brought about a remarkable reduction in her infant death-rate.

Some conception of the waste of human life that has accrued from the world-wide neglect of the rights of the little child to live can be obtained from some interesting figures that have been gathered in England. If the death-rate of 1914 had obtained in England for the last forty years England would have today, in addition to her present available fighting force, 1,300,000 men between the ages of eighteen and forty years; and had England been able to maintain her birth-rate of forty years ago through this same period these figures would have been doubled. Another group of English figures bears upon this careless wastage of life. In 1915 there were 875,000 babies born in England. On the basis of the experience of recent years 100,000 of these were due to die before the end of their first year of life and an additional 100,000 before the end of the fifth year. In the same year—1915—the stillbirths and misearriages in England amounted to 120,000. Therefore, out of a potential birth-rate of 995,000, 320,000, or almost one-third, were doomed to die before the end of the fifth year. It is a perfectly safe estimate that one-half of these fatalities could have been prevented—in other words, that with ideal health conditions established England could have added to her population 160,000 lives in 1915.

The foregoing figures are taken from English reports rather than our own, because we have no figures for the entire United States—only 31 per cent. of our population comes within what is known as the birth registration area—that is, the area in which the standard certificate is used and at least 90 per cent. of the births are reported.

If there was a great destruction of human life before this war, what can be said of that which has happened since it began. The figures are appalling, and they emphasize the fact that we must dwell upon today and use as the basis of our fight for the rights of the child to live, viz., that the life of the child has a greater economic value than it has ever had before.

The plea of the moral right of the child to live has had but little influence upon the minds of men. Perhaps they may understand the meaning of a child when measured in terms of dollars and cents.

When this war was called into existence by the lord of Kultur it resulted in the sudden withdrawal of millions of men from civil life and the establishing of conditions in each of the belligerent nations that led to a rapid decline in the birth-rate. This decrease has varied in the different countries, but it has been very great in all of them.

At the beginning of the war, as would naturally be expected, the interest of the people and their governments was centered upon problems that were directly connected with the development and maintenance of their armies. The result was that the problems of civil life were neglected. The welfare agencies that were dependent for their existence upon the voluntary effort and contributions of the people lost both their workers and their finances. The contributions

to war loans, the maintenance and carrying out of the work of institutions such as the Red Cross left the ordinary private agencies of civil life stranded. The withdrawal of physicians and nurses trained and working on public health problems handicapped the activities of governmental institutions. Some private agencies went out of business, all of them curtailed their work, the governmental departments became less efficient, as the result of which sickness and death among infants and children increased by leaps and bounds. This experience was common to all belligerent countries.

Coincident with this the casualty lists began.

In short, the various nations found themselves facing the solution of these problems:

1. A decreasing birth-rate.
2. An increasing death-rate.
3. An appalling destruction of adult life on the field of battle.
4. A great maiming of men, thousands of whom were totally incapacitated, and many thousands more who were so wounded as to be only partially capable in the years to come.

What was to be done?

Manifestly the deaths and wounds from battle could not be materially lessened as long as the war continued, and an increase in the birth-rate in war times was impossible. Indeed, as men fall in battle and new men are called to replace them the birth-rate naturally decreases still further.

There was one possible way, however, of stemming the tide of destruction, and that was by so reducing the infant death-rate as to at least in part compensate for the loss in population that the other conditions were producing.

To this end each of the various governments is bending its energies, with varying degrees of success.

What will be the fate of the smaller countries that have quaffed the cup of Kultur served them by the Hun—some with her arm around them, others with her mailed fist against their faces—no man can tell. The clouds upon their horizons are black and they seem to have no silvery lining.

Russia is now engaged—under the gentle guidance of sweet Germany—in destroying herself. Her outlook is unpromising.

Of Italy and Austria we have no authentic information as to the amount of sickness or number of deaths in civil life at any age period. We are entirely justified, however, in assuming, from our knowledge of the conditions in general in civil life, that morbidity and mortality are both high in all age periods.

We have no recent information from the land of the Boche, but prior to the severance of diplomatic relationships with Germany we knew that her infant mortality rate which had been lowered was increasing so fast that the government had forbidden the publication of statistics, and that her birth-rate was very low, being 40 per cent.

less in 1916 than the birth-rate of the year immediately preceding the war—a reduction in round figures of 735,500. We knew further that women and children were being exploited that the war might be won.

In August, 1914, the Reichstag, in order to be freed from all trammels and have opportunity to advance the cause of Kultur, passed an emergency law giving the Chancellor power to set aside all the factory laws and regulations for the well-being of women, young people, and children employed in factories.

An investigation made in September, 1915—a year later—by the German Metal Workers' Union as to the conditions under which women were working, revealed appalling conditions; 36 per cent. of the women were found to be working fifty-four hours in the week and 63 per cent. over sixty hours. In many cases they worked from seventy-five to eighty-four hours, and the shift workers sometimes worked from seventeen to twenty-four hours at a stretch.

Regarding France and England we have more accurate information. The experiences of France are probably suggestive of what is transpiring in Austria, Italy, and possibly in Germany. At the same time they stand as a warning of the destructive possibilities of modern warfare.

France has been an invaded country since the beginning of the war. The blow that struck her was severe, and in its suddenness unexpected. Her initial casualty list was enormous. These facts, together with the overwhelming problems of the future, demanded the immediate utilization of every resource to place the army in a position to withstand the onslaught of the Hun. The inevitable result was neglect of the civil population and the withdrawal from civil life of the people qualified to maintain the welfare of the civilian. From the very beginning of the war the drain upon the medical and nursing professions was most severe. As the war progressed this situation became more and more serious until in February of the present year there was only one physician to every 8000 of the civil population and no such thing as a public health nurse outside of military service. Until recently, when the American Red Cross began to supply physicians and nurses, the health of the civil population was largely under the guidance of volunteer workers. France has never been able to react from the effect of the original blow.

What has been the result? The birth-rate in France in 1913 was 18.8 per thousand of the population. In the year 1916 it reached the astounding figure of 8.6 per thousand. This meant a decrease of approximately 405,294 births in a single year. Before the war the birth-rate equalled the death-rate. It has been estimated that this decrease in the birth-rate plus the increase in the death-rate in civil life and the added death-rate of military life will result in a reduction in the population of France for the year 1917 of 790,000, or more than three-quarters of a million. Her losses in 1916 were 788,000—only 2000 less than the estimated loss for the present year.

What has happened in England?

England has never been invaded. Her military development has been more gradual, which means that there has been a less rapid withdrawal of men from civil life. This procedure has had a less sudden and severe influence upon her birth-rate. In general, England has had a much better opportunity to adapt herself to the changing conditions. Nevertheless, in England, as is inevitable in any warring country, the casualty list and the decrease in birth-rate has happened. As has been said, England also experienced a sudden and striking initial increase in her infant death-rate, due to the same causes that were active in other countries, namely, the diversion of the interest and activities of the government and her people from the problems of civil life to the preparation of her army for military service.

In 1914 the infant death-rate in England and Wales was 105 per thousand living births, in 1915 it was 110 per thousand—but England saw the handwriting on the wall. The decreasing birth-rate, the increasing infant mortality, the civil deaths of other age periods, and the fatalities of battle were spelling depopulation. Her response to this situation was the perfecting and extending of her machinery to save the lives of her infants.

All government agencies were rendered more efficient, her health visitors were increased to 1 to every 500 infants born, and all of her private welfare agencies were voted grants of money, so that instead of curtailing they might extend their work. The result has been most striking. England's infant death-rate for 1916 was reduced to 91 per thousand living births, a saving over the previous year of 19 lives in every thousand born.

In this way England has been able, in large part, to compensate for her decreasing birth-rate.

If England is able to maintain this standard and end this hellish war with a relatively small decrease in her population, of all the European countries involved England's future is the most assured. There will be less shortage in man power in the years to come, and England will have established on a firm basis the machinery with which to ensure to the children born to her a place in which they can dwell in safety.

In every warring country the number of children born will continue to decrease in proportion to the number of men called to arms, the number of women taken into industry, and the increase of poverty in the essentials in life.

The casualties of battle—the killed and the wounded—will continue as long as the war holds.

The influence of these new conditions added to the factors which contributed to sickness and death before the war can yield but one result—a rapid decrease in population.

It is such a procedure as England is following that will compensate in part for such losses and justify the statement—"that the answer to the question, 'Who has won this war,' will be given twenty or thirty years from today." Naturally it will be the country that so maintains the nutrition of its people to yield the highest degree of efficiency and most nearly maintains its rate of increase.

And now our beloved country is at war. The experiences of other warring countries are soon to be our experiences. The present plan of our Government calls for an army of 5,000,000 men. When 5,000,000 men are taken out of civil life the influence upon the birth-rate of the land will be tremendous. It is no argument to the contrary that the majority are unmarried. Unmarried today, yes, but many of them would have been married in another year.

The casualties of battle are coming to us too. Soon the black band of mourning will be common to our eyes and soon our tears will be shed with the blood of our sons.

It is easy enough to talk of the casualties that are coming to us. It will be another thing to face them. Do you ever stop to think upon what we are likely to face? Do you realize that Russia with her millions upon millions of men to whom the Allied nations looked for powerful and continued help has been eliminated from this war? Do you know that Italy is weakening and that noble France is fighting on sheer nerve today? Finally, do you understand the meaning of these things?

Upon the shoulders of England and America will fall the greater part of the burden of this conflict in the years to come. What that burden has meant to the nations that have borne it since August, 1914, we know.

Most assuredly will we add to our lowered birth-rate the casualties of battle.

Deaths as they have happened before the war must continue.

God forbid that through neglect of our civil problems we should add to this list an increase in the death-rate of the civil population—especially of our infants and children!

Without war we have a child problem in the State of Pennsylvania.

In 1915, with a death-rate of 110 per thousand living births, we had the distinction of having next to the highest infant death-rate of any of the States in the registration area.

We also harbored the town of Shenandoah, which, with a death-rate of 196 per thousand living births, had the highest rate of any town or city in the registration area.

What is to happen to us in Pennsylvania if by neglect we lessen the efficiency of the manifestly inadequate institutions that have prevented our death-rate from going higher than it now is?

Dare we become so deeply involved in the problems of war as to neglect this most vital of our civilian problems?

England's neglect in increasing her infant death-rate from 105 per thousand living births in 1914 to 110 per thousand in 1915 added to her casualty list for that year the lives of 4375 infants under one year of age.

For every child that dies four are ill. So England's increased casualties were not *only* of the dead, but, in addition, there were four times 4375 or 17,500 wounded.

This country faces a grave situation. Its manpower is threatened. Immigration has ceased and probably will never again be a very potent factor in the increase of our population. We have established literacy laws which in normal times would have caused a great decrease, but what is of much more significance the loss of men in the countries which were once the source of our supply has been so great that these countries are considering the advisability of placing a permanent embargo upon emigration which will practically end this source of increase.

We will be dependent therefore upon our own resources.

Today we have not enough men to do the work of our industries. If men are to be killed in battle or maimed for life, if our birth-rate decreases and by any chance our infant death-rate is permitted to increase, we will create conditions that will require generations to overcome.

What can we in Pennsylvania do to offset this possibility? War is upon us—our men are falling on the battlefield—we cannot check the guns of our common enemy—the deaths and wounds of battle are inevitable.

As in all the rest of this warring world our birth-rate will decrease in proportion to the number of men that are called to fight in the cause of liberty. This is the law of battles.

Is there nothing that we can do to protect our beloved country against the influences of these inevitable things?

The answer to this question has already been given.

The present infant death-rate in Pennsylvania is 110 per thousand living births. New York City, with its desperate problems of alien population, poverty, overcrowding, immorality, and crime, maintained an infant death-rate for the first seven months (up to and including July 28) of the present year of 83 per thousand living births.

If that is possible in New York it is possible in any great city of the land, and should be easily attained in the great cities of Pennsylvania. In our smaller cities and rural districts we should establish the figures of Australia, Sweden, Norway, or even New Zealand, in which in the year 1913 the infant death-rate was 38 per thousand living births. If but 25 per cent. of the possible 50 per cent. reduction could be accomplished in Pennsylvania we would save each year the lives of 27 babies in every 1000 born, or, in round figures, 5938 babies' lives.

By what procedure can such results be reached?

The basis of all health work is education. England was able to reduce her infant death-rate from 110 per thousand living births to 91 in a single year by multiplying her educators. The Government financed every private agency of standing and multiplied her health visitors—the women who go into the homes of the people to tell them how to care for their babies and children—so that she had 1 to every 500 children born. New Zealand attained her results by the education of all classes—especially of the mother in the home—and in answer to this question which I recently addressed to Dr. S. Josephine Baker, Director of the Bureau of Child Hygiene in New York—"To what do you attribute the striking reduction in the infant death-rate in New York accomplished in 1916?" I received the following reply:

"The feature of our work which I feel to have been of most value in 1916 in reducing the infant death-rate was the widespread emphasis that was given to the education of the mothers. You will remember that during that year we had the epidemic of poliomyelitis. Mothers became more than ever anxious to get information which would help them to care for their babies. This gave us an opportunity to carry on a very definite health campaign for the prevention of infant mortality, and we made every effort to get the coöperation of every agency in the city which was engaged in any work which related to infants. The results were most encouraging, as we had 1052 fewer deaths of babies under one year of age in 1916 than in 1915 and 324 fewer deaths of children under five years of age in 1916 than in 1915, notwithstanding the fact that the greater proportion of our deaths from poliomyelitis in 1916 were in children under five years of age."

Whatever is to be done in Pennsylvania must be accomplished also through the education and coöperation of all classes of society, but above all through the education of the mother in the home. Unfortunately we cannot do what England has done. We are dependent upon our State and Municipal Governments for our appropriations. Our State bodies do not meet annually, and therefore we cannot secure financial assistance from the State until our Legislature is in session and even then we have the barrier of politics to penetrate.

Ultimately governmental assistance will be given, but we dare not wait. We dare not neglect the problems of our civil population.

The one that is most urgent and most promising of results is the infant mortality problem. Infant mortality is a community problem, and therefore is an index of the health of communities. The conditions that cause sickness and death among infants also cause sickness and death in all age periods. Therefore the removal of the agencies which cause infant mortality contributes to improvement in the health of all the people.



For the present the solution of this problem is largely dependent upon the services of the volunteer.

It becomes our duty as citizens—just as great a duty as that we owe to any of the activities directly connected with the creation and maintenance of our armies—to give of our time and our money to the institutions that have been or will be created for the protection of the lives of our children. Let us not add to the casualties of battle the casualties that will inevitably follow the neglect of these little ones. Pennsylvania is now calling to her citizens to see to it that her people are protected in such way as to make it possible for them to give the best that is in them to the work they are doing so that the highest efficiency at home may contribute to the efficiency of our armies abroad. What will be your answer?

When Harry Lauder was in Philadelphia a few weeks ago he said that when he went into the trenches and asked the boys how they were the answer was, "How are we? Oh, we are all right; but how are the folks at home?" "*How are the folks at home.*"

Do you believe they want the answer to that question to be the babies are dying, the children and grown-ups are sick, the efficiency of the workers has been reduced, and the supplies that should come to you will be delayed because the civil population has been neglected?

Remember what they are sacrificing that we may be saved. It is not alone the giving up of the home and the loved ones that dwell there, but the supreme sacrifice of life itself.

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## THE PROPHYLAXIS OF MALARIA.

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FOR an Army man, venturing into print, especially at this time, it seems hardly excusable to write on any subject not related in some important way to the existing war. Malaria has not been reported as having given great trouble along the Western front, where our Army will no doubt be mainly employed, yet it seems well to review our knowledge of the subject at the present time. We have not yet received the complete reports of the disease incidence there, and it may have been greater than we know. It is quite conceivable that malaria might appear in a troublesome way if any carelessness were shown in our own sanitary arrangements, and it certainly seems important, or liable at any time to become important, in view of the many large cantonments and camps that we are now preparing in this country for our big new American Army, some of which are of necessity situated in districts not entirely free from suspicion of malarial endemicity.

I wish, also, to emphasize a point which will be new, I think, to many of our lately commissioned doctors, and that is that the most necessary thing in their sanitary work is to impress on the minds of the line officers and soldiers the immense importance of little things, as compared with great ones, in their effect upon the ultimate success or failure of military campaigns. This idea is not a fanciful one—quite the opposite. Many of these officers, some of them of high rank and scientific training, who certainly ought to have known better, have in our past wars affected to sneer at such things as insects and germs. They somehow do not seem to be able to realize that most of our sorrows in this world are due to germs, directly or indirectly, and that many of their injurious consequences can be prevented by extremely simple and easily executed means.

The subject of malaria offers a good—perhaps the best and easiest understood—text for the educational work referred to. Much has been written about malaria, especially in recent years; so much that it seems that all medical men must now be thoroughly posted on the subject; but perhaps it has not been too extensively considered from our present point of view, and the story of Panama and the sanitary triumphs there, as an example for future effort, cannot, I think, be too often told. Possibly the reader may not object to considering a few of the impressions of an eyewitness of the work done there.

In war, to repeat, we have to fight the infinitely little as well as the overwhelmingly great. At one and the same time, medical service in the field has to repair the mangling of the human frame by man-sized explosive shells or other 42 cm. effects, and to fight fleas and flies, lice and mosquitoes, as well as the rodent carriers of some of these insects. It is probable that the gigantic creatures which dominated sea and land in prehistoric times were ultimately destroyed by pathogenic bacteria and parasites, perhaps even by ultramicroscopic filterable organisms in some cases. The huge dinosaurs, pterodactyls, crocodiles, and saber-toothed tigers, while warring on each other, could be extinguished in the end only by adversaries so contemptible in size and shape that they were apparently negligible as competitors in the fierce struggle for existence.

H. G. Wells has a story of the invasion of the earth by giant inhabitants of the planet Mars, who descended from the skies encased in shell-shaped capsules. Upon emerging from these the giants proceeded to devour all human beings in sight as being something merely "good to eat." A reign of terror ensued. Man could not cope with such antagonists as these. Finally the cannibal race began to die out and eventually disappeared. The bacteria did the business. So, too, up to recent times the most formidable enemies of huge armies have not been the shells and bullets of the opposing forces but the pathogenic organisms found in the soil and on the bodies of "varmints and vermin." "Every bullet has its

billet" is a well-known military aphorism, but until very recently the Napoleonic idea that "it takes a man's weight in lead to kill him" has held good. So many thousand bullets fall wide of the mark and find their billet in the ground. But thousands of pathogenic organisms may find their billet in the body of a single soldier in the trenches.

**HISTORICAL NOTES ON THE SUBJECT.** In ancient times there was considerable intuitive feeling concerning the relation between insects and disease. Amulets against fleas and flies were common in Egypt and Mesopotamia. One of these, a cylinder seal, with the fly-symbol of Nergal, the god of disease and death, is in the Pierpont Morgan collection. In the Book of Kings, Beelzebub, the god of flies, is approached by the sick Ahaziah.

Garrison,<sup>1</sup> quoting Sir Harry Blake, says that the theory that mosquitoes can transmit malarial fever was indicated even in the Sanskrit *Suśruta*. It was a far cry, however, to the year 1883, when the hypothesis was more definitely stated by Dr. A. F. A. King, of this city. Sir Patrick Manson had recently proved the conveyance of filariasis by the mosquito. Laveran, a French army surgeon, in 1880, had described the causative organism of malaria—the plasmodium—discovered in human blood. Ronald Ross, of the Royal Army Medical Corps, a little later completed the proof of the mosquito transmission of the disease.

I should like to invite attention at this point to the remarkable set of experiments which, in confirmation of the laboratory findings, practically proved the connection of malaria with the mosquito. These were conducted by Drs. Sambon and Low, in the summer and autumn of 1900, on the Roman Campagna.

The experimental party occupied a screened hut in the malarial section of that notoriously malarious region, on the banks of a canal swarming with *Anopheles*; that is, from late afternoon to morning they kept themselves absolutely screened in the cottage—going about in the daytime as they pleased, even allowing themselves to be soaked through in the rainy season. They could observe the *Anopheles* mosquitoes trying to enter the screened windows, which, except for the screens, were kept entirely open to the marsh air. The result was that none of the party contracted malaria, though the people in the neighborhood, not protected by screening from the mosquitoes, rather uniformly developed symptoms of ague. As a control experiment an infected mosquito was sent to London, where there is no malaria, and allowed to bite a healthy man, the son of Dr. Manson. He contracted in due time a well-marked attack of fever, and the parasites were found in his blood.

There are many references to malaria in the histories of campaigns, some of these dating back to the earlier periods of civilization. Of

<sup>1</sup> History of Medicine, Philadelphia, 1917, 2d edition, p. 617.

the later ones, of which we have the fullest accounts, some resulted in great disaster. One author holds, with apparent reason, that the epidemic in the Greek camp before Troy was malaria, as the neighborhood was evidently very marshy.

We learn from Hippocrates, in his descriptions of malarial cachexia and other forms of the disease, that so early as 400 B.C., Greece was very malarious. Catastrophes in war are recorded, including a severe outbreak in Attica during the Peloponnesian war.

The disease was evidently known to Xenophon, who said (and he gives good advice, it will be noted): "If you intend to stay some time in one place you must not neglect the health of your camp. It is an easy matter if only care be taken, for the inhabitants never cease talking about unhealthy and healthy regions, and their physique and complexions are trustworthy evidence in both cases."

It has been seriously advocated, and with much show of reason, that malaria played one of the largest parts in the decline of the ancient Greeks, both in peace and war.<sup>2</sup> Many citations from non-medical and medical writers, including Hippocrates, signify the great prevalence and importance of the disease. The effects are noted from about 400 B.C. on. A sort of vicious circle is described which it may be worth our while to note. Malaria in the rural districts sapped the health and energy of the inhabitants, children, the potential progenitors of new generations, being naturally the chief victims. The country was deserted except by the diseased and feeble remnants of the population, and the mass of the people removed to the cities, with consequent loss to agricultural industry, the natural foundation of the wealth and prosperity of a nation. City life gradually led to the decline in physique of individuals; habits of inertia and laziness supervened and superstition became rife, as evidenced by the vogue of dream oracles and astrology. "Back to the soil" propaganda naturally resulted in a few generations, and the circle started over again. It appears that there was a silver lining to the cloud, in that increased respect for women resulted from the necessary assumption of the duties of nursing the sick by the weaker sex, generally the wives and female relatives of the afflicted individuals. The theory of the deleterious effects of urbanization on national progress, if true, points a conspicuous moral for us today.

A modern Greek author says, in relation to contemporary conditions in Greece, that "malaria is the sword of Damocles hanging above our heads. It chooses the rising generation, drains the strength of the adults, lays waste our fields, and weakens the arms of our warriors. Numbers of soldiers have fallen victims to fevers." The Greek Army was badly infected with malaria as late as 1909.

<sup>2</sup> Jones, W. H. S.: *Malaria and Greek History*, University Press, Manchester, 1909.

On account of malarial fevers the Gauls under Brennus had to forego the otherwise certain capture of Rome.

We lack the space to recount the ravages of this protean disease in the Middle Ages, and must therefore resist the temptation to cover its history more fully. Mention of a few notable instances in modern times will not, however, come amiss in relation to the purposes of our paper.

The Walcherian expedition of the English, about one hundred years ago, is a notable example: 10,000 men out of 15,000 were actually sick at one time, and with a few days' fighting and two or three hundred casualties there were several thousand deaths from malaria in a four months' campaign. This shows, according to Melville, that our military strategists should take some notice of the science of epidemiology.

In the Burmese war of 1825-6 the British forces were practically made ineffective by the country's "malignant fever." Over 5000 European and native troops were struck down, and it was said that "Everyone who was not dead was in hospital."

The campaign of the French in Madagascar, in 1895, was even more disastrous. They had no important military reverses; in fact, carrying out the march exactly as planned without serious opposition by the enemy. They lost less than a score killed by wounds, but some 5000, about one-third of the total force, died from malaria.

In our own Civil war there were about 800 admissions for malaria per thousand of the forces engaged, though the mortality was not startling, owing to the benign type of most infections. Think, however, of the invalidism and the interference with military operations. "Chickahominy fever" it was called. It will be remembered how the French under De Lesseps failed in digging the Panama Canal. Partly owing, no doubt, to bad financiering, this failure was mainly due to the extreme sickness and mortality among the laborers from various diseases, but principally from yellow fever and malaria. In some months the annual mortality per 1000 ran up to about 240. When one considers the amount of sickness and invalidism that these figures show must have been present, and the resultant great expenditure of money, it is easy to see that the carrying out of an engineering enterprise of such colossal magnitude as the digging of a ship canal between the two oceans became absolutely impossible.

At Santiago, in our late war with Spain, malaria struck about half our force at the same time; the parasites were of the malignant variety and the infections all severe. If military conditions had not permitted the return of the expedition to the United States when it did return our Army would most probably have been practically annihilated; and if the Spanish had put up a stronger resistance

\* Duncan, Andrew: *Prevention of Disease in Tropical Campaigns*, London, 1888.

than they did the whole course of the history of that conflict might readily have been changed.

How are we to avoid similar occurrences in the future? Perhaps we will not; we seem in the Army often quite slow to profit by past experience. I refer to our Army as a whole, not to the Medical Department. If we were forced to invade Mexico tomorrow we might possibly have experiences quite similar to those I have described, and we will no doubt have much invalidism and consequent interference with military training in some of our Southern camps if we "don't watch out." At any rate some of us will be called upon to give advice, and it is this phase of the situation that constitutes the *raison d'être*, if any, of this paper.

I would say in passing that the present condition in the United States Army with regard to malaria is quite encouraging, except in the Philippines, where a badly infected native population in connection with a lack of screening in barracks and quarters keeps up the malarial rates. The admission rate for the entire Army in 1915 was only 25 per thousand.

Present reports from Panama show a very different picture from that outlined above. The general mortality on the entire Isthmus of workmen and natives alike has been cut down to about that of our American cities, and among the employees of the Canal Commission, and especially among the Americans and their families there, to very much below our rates in the United States (about 7.5 per 1000). Of course, all the resources of modern sanitation were utilized in the work, but the most significant and important factor by far in the marvelously successful operations has been the antimosquito work. We of the Army Medical Corps take great pride in the fact that the sanitary work on the Isthmus was, from its inception, entirely under the charge of one of our own men, Colonel (now Major-General) William C. Gorgas, who had previously been instrumental in banishing yellow fever from the Island of Cuba. On the basis of the Cuban experience he devised the methods used at Panama, organized the personnel and established the equipment of the Sanitary Department there, and had for ten years close personal supervision over all the workings of the department. He has himself told the story of the work in a modest but most interesting way.<sup>4</sup>

Many of his subordinates have done excellent work there, in one way or another, but having been myself on the spot, I do not hesitate to say that the success was due entirely to the inspiration drawn from General Gorgas himself; that without the wonderful administrative ability he developed and exercised there even our modern scientific methods would probably have resulted in failure. This is in passing, however, and need not discourage us in other

<sup>4</sup> Gorgas, W. C.: Sanitation in Panama, New York, 1915.

attempts. The parents and relatives of our new American soldiers may, I think, rest easy that under his administration of the Medical Department in this war the greatest dangers from military service stand every possible chance of being successfully overcome.

How was this work carried out? It would take a long time to tell it in detail, but we can cover the general principles, perhaps, in a few pages.

I had myself two years of practical work along these lines as executive officer and general inspector for the Sanitary Department at Panama, and I should like to record the impression I received as to the relative value of the different measures that were used there.

THE IDENTIFICATION OF THE MALARIAL MOSQUITO. But, first, we must digress a little here to say a few words as to the identification of the definitive host, the *Anopheles* mosquito. I think that most of the published books and articles on mosquitoes are too scientific or too detailed for the purposes we have in view here.<sup>5</sup> A few simple facts in regard to the biology and the life-history of these insects are all that are necessary for the practical worker in sanitation, and these I shall try to supply as briefly as possible.

The mosquito in its life-history undergoes what is known as a complete metamorphosis. The egg hatches out into a voracious, predatory, and rapidly growing larva, and next there appears a non-growing, non-feeding stage in which the organism is called a pupa, or nymph. From this latter emerges the full-grown insect or imago.

We should at least learn to recognize the larval and full-grown forms. The pupæ of the different genera appear, to ordinary observation, very much alike and their distinction may well be left to the expert. The pupal stage lasts from about one to three days. So with the ova, which, it will be remembered, are always laid on or near water. The eggs of the genus *Culex*, which includes the ordinary domestic mosquito, appear in black, scooped-out masses about one-fifth of an inch long on the surface of the water, known as egg rafts (Fig. 1).

*Anopheles* eggs, on the contrary, are usually laid single and tend to cohere, with extremely slight cohesion, however, in triangle and ribbon patterns (Fig. 2). The length of the egg stage varies with the temperature and other external conditions, being about two to four days for *Anopheles*.

The larval stage is that of the well-known "wiggle-tails." The larva of *Culex* has a breathing tube or respiratory siphon which projects off at the caudal end at an angle from the axis of the body and ends in four flap-like paddles. It is long and slender in shape (Fig. 3).

<sup>5</sup> The most practical and yet informing work on this subject is: Mosquitoes: How They Live; How They Carry Disease; How They are Classified; How They May be Destroyed, by L. O. Howard, New York, 1901.

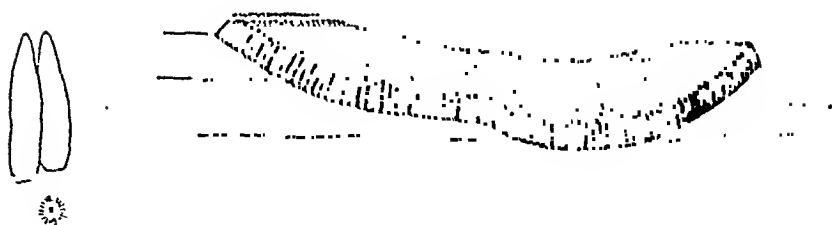


FIG. 1.—Egg mass of *Culex pungens*; enlarged; with individual eggs, still more enlarged, at left. (After Howard.)

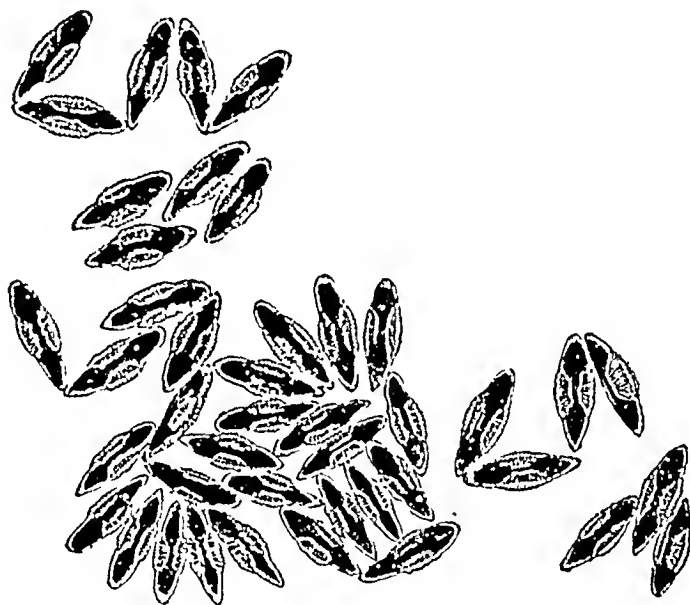


FIG. 2.—Egg mass of *Anopheles maculipennis*; enlarged. (After Howard.)

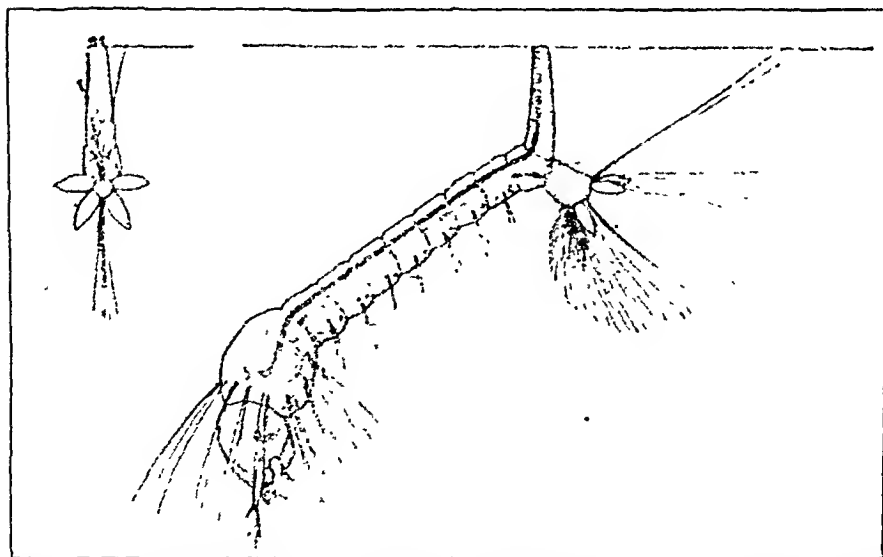


FIG. 3.—*Culex fatigans* larva in breathing position at surface of water; enlarged. (After Howard, Bull. United States Dept. Agr.)



The breathing-tube of the *Stegomyia* larva, on the contrary, is short and barrel-shaped. The body of the *Culex* larva when it comes up to the surface of the water to breathe hangs down at an angle of about 45 degrees, while the *Stegomyia* hangs much nearer the vertical (Fig. 4). This last fact, coupled with the shape, is a

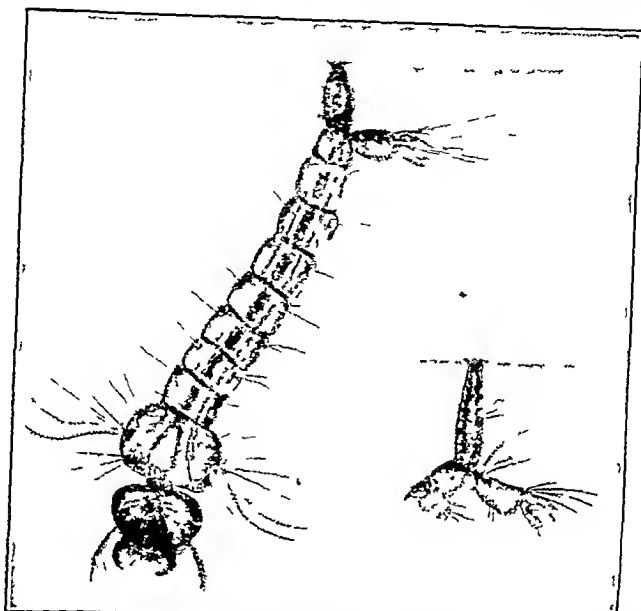


FIG. 4.—Larva of *Stegomyia calopus*. Inset: breathing-tube of *Culex* larva; both enlarged. —(After Howard)

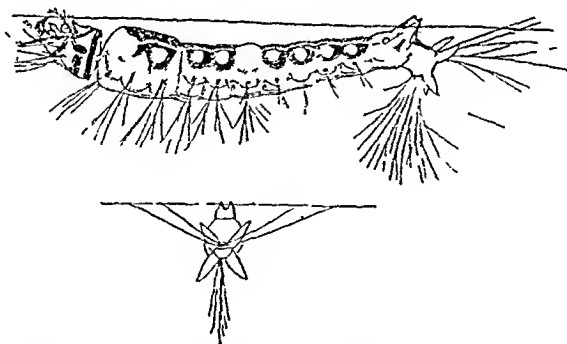


FIG. 5—*Anopheles maculipennis* larva, showing breathing position at surface of water; enlarged. (After Howard, Bull. United States Dept. Agr.)

rather important point in the practical differentiation of the larvæ, and after a little experience one can pick them out with confidence. In the two kinds of larvæ just described the head is relatively large.

The larvæ of the *Anopheles* are so entirely different from the others that there is little danger of confusing them. They are much smaller in size than the others and are of a darker color. They rest parallel with the water (Fig. 5). They dart around in a jerky sort of way

on and near the surface of the water instead of coming up from the bottom for air, breathing a while, and then slowly going back again. They look like little dark-colored short spicules. There is no respiratory siphon at all, and the small-sized head, if one examines very carefully, can be seen to be rapidly turned about 180 degrees when it stops and starts to breathe. The duration of the larval stage is a week or more, according to circumstances.

All the stages of development in the *Anophelins* occupy, on the average, about two weeks, with a minimum of, say, eight days in the tropics. The usual method of hunting larvæ, especially the *Anopheles*, is to inspect carefully the surface of the water and take "dips" with a tin cup when anything suspected is seen. A closer and more accurate examination can then be made, if necessary employing a hand lens.

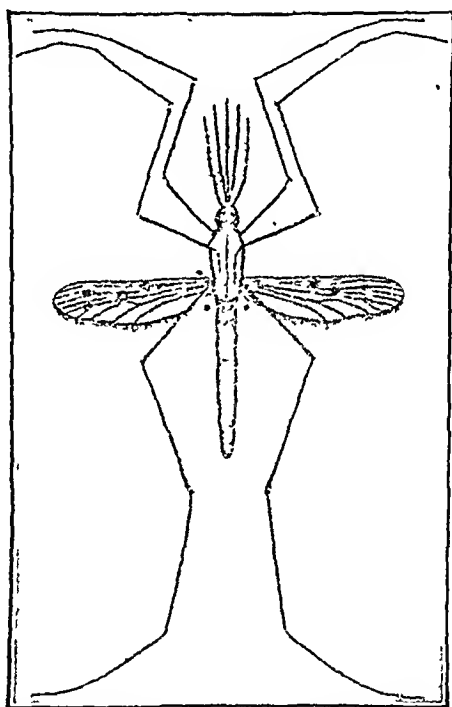


FIG. 6.—*Anopheles maculipennis*, female; enlarged. (After Ludlow.)

In regard to adults, and this is the really important point in mosquito differentiation—that one may really know an *Anopheles* mosquito when he sees it—all mosquitoes of importance medically have, in the male, palpi (or feelers) as long as the proboscis or longer, but only in the genus *Anopheles* is this true in the case of the female (Fig. 6). In all other genera the palpi of the female are considerably shorter than the proboscis. Close examination with the naked eye will show this, but a low power hand lens will help one, at least in his early work.

It may be parenthetically stated here, as the reader no doubt knows, that only the female mosquito sucks blood, which she uses in the development of her ova, otherwise and in the case of the male they live on the juices of plants. In other words, it is only the female *Anopheles* that bites and transfers the malarial parasites. In this instance, therefore, actually as well as potentially, "The female of the species is more deadly than the male."

The palpi are thus of the utmost importance in differentiating adult mosquitoes. The proboscis is straight in all mosquitoes of importance medically. The antennæ of the male in all genera show a profusion of long, silvery hairs (like "whiskers"), the female only a few downy ones, thus offering an easy method for the determination of the sex of a specimen (Fig. 7).

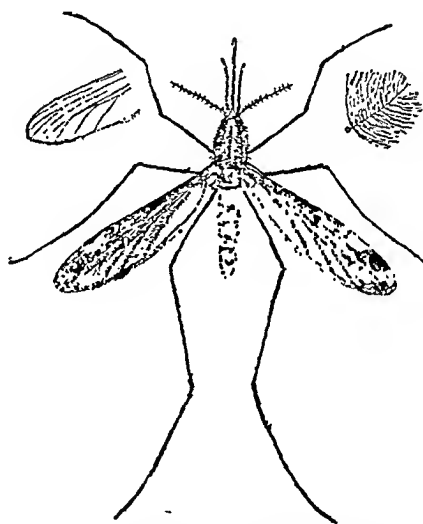


FIG. 7.—*Anopheles punctipennis*, female, with male antenna at right and wing tip showing venation at left; much enlarged. (After Howard.)

The adult *Stegomyia*, if once closely examined, cannot be confused with any other mosquito. The yellow fever bearing species is now called by entomologists *Aedes calopus*. The brilliant black and white coloring, the white bands on the legs, the "lyre" adornment on the thorax are all quite characteristic (Fig. 8).

Most *Anophelines* have black or brown patches on the wings, though the wings of some species are mottled yellow and brown (Figs. 6 and 7).

The most practical way, however, in which the *Anopheles* may be identified in antimalarial work as, *e. g.*, in the inspection of barracks, is the peculiar attitude it assumes when resting on a vertical surface or wall. This is very striking, and once seen cannot again be easily mistaken. While the *Culex* or *Stegomyia* rests with

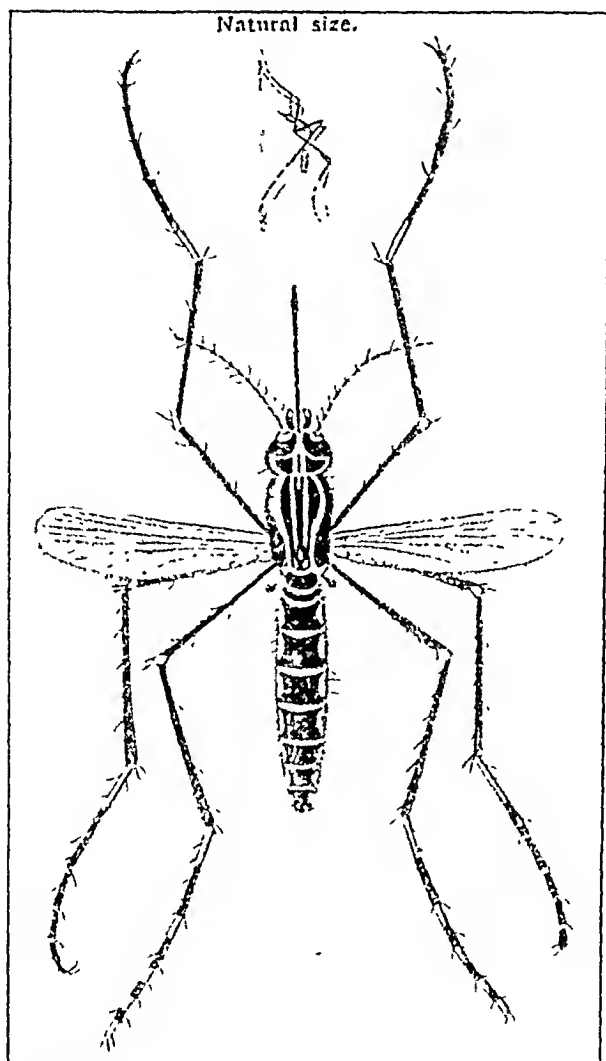


FIG. 8.—*Stegomyia fasciata* (*Aedes ealopus*), female; the yellow fever mosquito; enlarged. (After Ealand.)

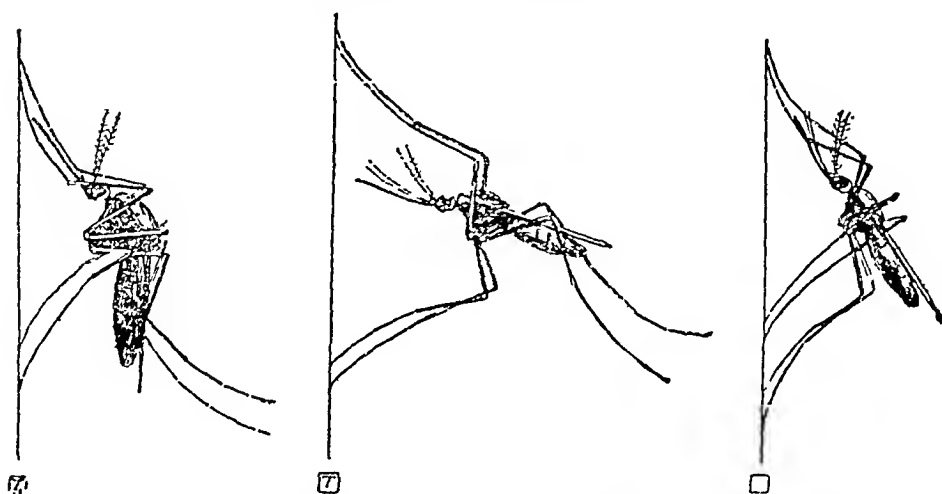


FIG. 9.—Resting position of mosquitoes; enlarged. (After Howard.)

the body approximately parallel to the surface, and usually in a sort of curved or humped-up position, the *Anopheles*, on the other hand, sticks straight out, or rather at an angle of about 45 degrees or so, with the front end applied to the wall. It looks somewhat as if a very slender brad had been driven, slightly, at one end in a slanting direction into the wall. This is rather a difficult thing to describe, but it is really a practical and not a theoretical difference. The positions are not at all alike, and one may, by practice, readily learn to differentiate them (Fig. 9).

We know that some disease-bearing variety is present when working in a malarial region. We attack all Anophelines indiscriminately, and of course measures directed against one kind will act on all, their habits and mode of life being practically the same, and though the one we happen to be examining may not be a malaria-bearing species, still the conditions which allow it to flourish may also permit the existence of other species. The determination of the exact species (or even the genus) of the *Anopheles* is rather of academic than of practical interest to us in the kind of work we are now considering. The finding of Anophelines in general is therefore more important in practical health work than the running down of special varieties. Wherever paludism and anophelism coexist there prophylactic work is necessary.

In inspecting barracks for adult mosquitoes it is customary for the inspector to take an electric hand flash-light and go around the walls of the building, looking them over carefully for the resting *Anopheles*. One soon learns to pick them out readily and a room can be gone over in this way quite quickly. They show a disposition to haunt the dark places and corners in the daytime, hence the frequent necessity for the aid of artificial light.

Let us next consider, briefly, the habits and mode of life of mosquitoes. First, the very important point of their flying distance. It cannot be said that this is as yet definitely settled. Theobald says one mile. By experimentation in the Canal Zone they were shown to have actually flown more than a mile. Craig, at Camp Stotsenberg, estimated it as two miles. Young says that, as a rule, they do not fly over 200 yards. The latest theory seems to be that mosquitoes fly to food; if there is none intervening they fly the longer distances. I think we may safely say, for practical purposes, that the flight is "a few hundred yards," omitting exceptional conditions.

The mosquito is often carried for long distances on boats and railroad trains. The possibly great importance of this fact in the spreading of disease can readily be appreciated.

Mosquito eggs will withstand considerable drying; Craig says also the larvæ of *Anopheles*, though others dispute this point.

Larvæ can remain under water as much as ten minutes or more at a time.

Mosquitoes are rapid breeders and pass through several generations in a year. They hibernate in both larval and adult stages, especially gravid females.

The bite of the *Anopheles* is much more insidious than that of the *Culex* or *Stegomyia*. The song is in lower key, and therefore often not heard.

Another important point of difference is the distribution of the larvæ in nature. *Stegomyia* breeds in receptacles in and around and near the house, "containers" we call them. It is a sort of domestic mosquito; a town-dweller; in fact, it does not get far away from human habitations. *Anopheles*, on the other hand, has very different habits. It inclines to swamps and marshes and may be found far from the haunts of man. We find its larvæ also in ponds and reservoirs and rain pools, in puddle holes, and hoof marks and wagon ruts in pastures and fields, even in sluggish-running streams, usually along the edges where the current is not swift, and where algæ, mould or green scum abound, the latter indeed being one of its favorite locations on account of its use of this kind of vegetable matter for diet as well as for protection. They are thus suburban and rural rather than domestic, like *Stegomyia* and *Culex*. Many species, including some disease-bearing ones, can breed in brackish water.

The Anophelins are attracted at night by lights to houses; they bite mostly at twilight or during the night, though this cannot be relied on as an absolute rule, as sometimes indoors they will bite in the daytime.

*Stegomyia*, on the contrary, is said to bite principally in the late afternoon, though it may take blood at any hour.

THE PROPHYLAXIS OF MALARIA. To take up the question of actual prophylaxis, it goes without saying that a necessary preliminary is competent and accurate diagnosis of the disease conditions with which we have to deal. When malaria is extensively present, of course the thing is evident even to the layman. In hospital work we rely on the associated laboratories; nowadays, too, for field armies, there is the modern development of the motor field laboratory with the necessary microscopic equipment. But that is all another story; it would take too much time to go into it here. As we know it is worked out along the general lines of (1) the symptomatology, especially periodicity, in the symptoms; (2) the microscopic examination of the blood; (3) the therapeutic test, *i. e.*, the effect of adequate doses of quinin on the subsequent course of the disease. Also we might call almost pathognomonic the palpable enlargement of the spleen, found so seldom in other acute diseases besides malaria.

There are a good many different ways of fighting malaria. Perhaps all the authorities on the subject, or anybody who has taken part in these campaigns, would enumerate about the same methods of procedure, though there might be some difference of

opinion as to their relative importance. I think the best, and certainly the most logical, classification, as it might be called, of these prophylactic measures is that given by Henry R. Carter,<sup>6</sup> who was one of the pioneers in this work at Panama and elsewhere, and we can do no better than follow his general outline here.

Since there are two hosts concerned in the perpetuation of this disease, man and the mosquito, it follows of necessity that if we had absolute control of either we could stamp out the disease in the locality in question. To explain: if every person harboring malarial parasites could be apprehended and isolated, and kept away from mosquitoes as long as any of the organisms remained in his blood, there would be no further infection for the insects to convey and the disease would stop. Similarly, if we could "corral" all the *Anopheles* mosquitoes, or in some way keep them away from their human prey, the malaria would no longer spread.

The former measure is, for obvious reasons, impracticable. So many people are carrying the parasites and getting around sufficiently well to attend to their ordinary business; again, the blood remains for such a long period of time potentially infected that it is naturally impossible to get thorough results along this line. So we must, in general, concentrate our resources on our second alternative and fight the mosquito; not neglecting, of course, to accomplish what we can in carrying out our more theoretical method with those patients of whom we do get control.

The eradication of malaria from a given community is a much more difficult matter than that of yellow fever, and for the following reasons:

1. The much more extensive distribution in nature of the *Anopheles* than the *Stegomyia* mosquito, as we have just seen—one breeding around the human habitation and generally confined to artificial containers, the other country-wide, as we may say. The adult *Anopheles* also flies farther than the *Stegomyia*—three or four times as far, according to Carter.

2. We know that there are only a few days at the beginning of his illness during which a yellow fever patient, if bitten by a mosquito, can transmit the infection through that insect. The malarial organism, on the other hand, remains infective in the blood for an indefinite period. Many natives carry the parasites in a latent way without symptoms, but nevertheless endanger the newcomer wherever there are chances of mosquito transference between them. So conditions make it necessary that we should concentrate our heavy ammunition on the mosquito. One result is that we can hardly hope to entirely eradicate malaria. What we try to do is to reduce it to what we may call a negligible point, to what humanitarian ends will allow, so that it will not interfere with our

<sup>6</sup> Carter, H. R.: Notes on the Sanitation of Yellow Fever and Malaria; from Isthmian Experience, Medical Record, New York, July 10, 1909.

economic undertakings, and so that the chances of infection of the newcomer will be brought to the minimum. We must spend a lot of time and money and energy in the fight—we naturally cannot spend all; we must use those things in addition for so many other purposes in life. This fact tends to make antimalarial work a little discouraging sometimes. No matter what we do we cannot hope to achieve perfect results (as we do in yellow fever) unless the place concerned is very small and the infected population not too large.

What methods shall we use to get the best results possible? Something about as follows:

1. To destroy the breeding-places of the *Anopheles*; to stop them at their fountain head as it were. If there were no breeding-places left there would naturally soon be no mosquitoes.

2. To kill at the breeding-places such of the larvæ as do nevertheless succeed in breeding.

3. To prevent the access to man of such mosquitoes as come to the adult stage in spite of our warfare on the larvæ.

4. To endeavor to so arrange it that the mosquitoes actually reaching man have had no chance to previously bite a person harboring the plasmodium; in this event, though they did bite, they would, of course, be harmless.

5. To protect our individual in some way, *e. g.*, by immunization, so that even if he is bitten by a mosquito capable of conveying the disease he will not contract it.

It will be noted that if any one of these measures could be successfully used in the order given it would prevent the necessity of carrying out any of the following ones; again, that any one of them, if carried out absolutely, would definitely stop the disease. The arrangement is also in the order of their importance. The first three of our remedies are aimed at the handling of the mosquito, the first two to destroy it, and the third to keep it away from man; the last one at the man alone; the last but one at both. In practice we must work along all these lines. Let us take up each of them in a little more detail.

1. *The Destruction of Mosquito Breeding-places.* The longer one works along these lines the more he will become convinced, I think, that this is by long odds the most important measure that we use in antimalarial work, also in the end probably the most economical. Mosquitoes breed in collections of water. If we remove the latter there can be no mosquitoes. Thus swamps and ponds and so on should be removed so far as possible. Small ponds and such like can be filled in. That settles the question for all time, but it is an expensive method—in most cases more than we can afford. Failing this, we can remove the collections of standing water by drainage, and this is, or should be, our mainstay in antimalarial work. No other measure begins to approach it in importance. Subsoil tile drainage with porous pipes is the most



satisfactory drainage method for this purpose, and I think in the end perhaps the cheapest; the cost of maintenance being very low, although the first cost is quite considerable. Next in order come drains lined with cement; then rock-filled or open ditches. The principal objection to these last two methods is the work necessary to keep them up. For this reason they should be used only when the work in the locality is to be temporary, say for a year or two, or where for some engineering reason, such as lack of fall, etc., the tile drains are impracticable. In the tropics the growth of vegetation is very rapid, and at Panama we found that open ditches had to be cleaned out about once a month—a great expense, as one can easily imagine.

As to the distance from habitations at which we should do this drainage work when, for instance, the whole country is *Anopheles* infected, it is, of course, hard to work out any definite rule that will fit all localities and conditions, especially as opinions are so much at variance as to the distance mosquitoes will fly. However, let us drain, say, all collections of water within 200 yards of villages and within 100 yards of houses. This is perhaps a little within the limits of flight of mosquitoes, but was found at Panama to give practical results, and it is evident we must consider the cost.

In looking out for possible *Anopheles* breeding-places we must not neglect to investigate the seepage water that comes out in the flat plains near the foot of hills. This gave us a world of trouble at Panama. It is controlled by proper drainage, the "intercepting" tiles being laid approximately at right angles to the line of flow of the seepage water. Under no consideration can cattle-tracks and such-like holes in fields be overlooked. The only satisfactory solution in many cases is to keep cattle out of the fields. At Panama the tiling is 6 inches to 10 inches in diameter, laid to grade, with open joints of about 1 inch; grade about 1 per cent. for the 6-inch tile and not less than one-half of 1 per cent. for 10-inch tile. Junctions of laterals with larger drains are made by curved "Y" joints.

2. *To kill the larvæ* in their breeding-places (where, for some reason, such as cost or expediency, we cannot do away with the water) we use kerosene or crude oil, which forms a scum over the surface of the water and thus prevents the possibility of the larvæ breathing when they come up to the surface. This is an excellent method when the conditions are favorable for its execution. We use about one ounce to every fifteen square feet of surface and renew about every twelve days or once a week in the tropics. On the Isthmus the laborers are supplied with a sort of knapsack sprayer for this work.

In many cases, the wind or rains washing the oil away, or vegetable growths in the water preventing the success of the kerosene method, we resort to the use of some chemical which, by mixing with the water, will actually poison the larvæ, a larvacide. We try to get

something which will not at the same time kill the animals which drink of the treated water. For a long time on the Isthmus we used a trade product known as Plinotas oil. It is effective on full-grown larvæ in ten minutes or less in a strength of 1 to 5000. The trouble with it was the cost and the fact that it was not standardized and thus varied considerably in strength. After much experimentation a local product was prepared which answered the purpose admirably. This is a mixture of carbolic acid, resin, and caustic soda made according to the following recipe: Heat 150 gallons of crude carbolic acid containing about 15 per cent. phenol to 212° F.; add 200 pounds of finely powdered resin, stirring until dissolved; add 30 pounds of caustic soda previously dissolved in water and boil for ten minutes, or until there results a dark emulsion without any sediment. Stir after the resin is added until finished.<sup>7</sup>

In running streams, and open ditches in particular, the supply of oil is best effected automatically. Drip cans are used, the oil being slowly and constantly discharged, through a hole containing a wick, upon the surface of the water.

One way of destroying larvæ is by the use of certain small fish which eat them voraciously, *e. g.*, the so-called "millions" of Barbadoes. There is no malaria on that island, and this is attributed by many to the fact that these little fish are so plentiful. The stickleback, the top-minnow (a species of *Gambusia*), and the common sun-fish have the best reputation in this respect. These will no doubt destroy the larvæ in small collections of water, but as a general method of fighting malaria my experience does not lead me to place much confidence in them, at least in the tropics.

3. *To prevent contact between mosquitoes and man* we use two principal methods.

(a) *Screening.* This is very important, particularly in the earliest stages of the work, when our other measures have not had time to show their full results. Details of screening are also of importance. Use a mesh of 18 to the inch and screen all openings. Make windows fixed and have doors open outward so as not to let in the mosquitoes that may happen to be on the outside of the door when it is opened. Put the door in a place where the light will not shine on it, as light attracts mosquitoes. Have as few doors as possible, to minimize the chances of mosquitoes entering. The best and really the most economical plan is to have a screened veranda all around the house, then none of the openings except the entrance door need be screened. Self-closing devices for doors are advantageous. Best of all is a screened vestibule with double doors.

In the tropics especially it is a measure of economy to use the best copper gauze for screening (the wire should contain at least 90 per

<sup>7</sup> For minute details on this point, and all the methods discussed, see *Mosquito Control in Panama*, by J. A. LePrince and A. J. Orenstein, New York and London, 1916.

cent. copper and not more than one-half of 1 per cent. iron). It is quite practicable to screen railroad cars and even tents when these are used for sleeping quarters.

In screening a building it is, of course, necessary to look out for cracks, knot-holes, and such other apertures as might admit mosquitoes. The mosquito net is of much less value than house-screening, but can be used as an additional precaution, or when, for any reason, one has to sleep in a tent or unscreened house.

(b) *Brush-cutting*, also the removal of high grass, is necessary, as it affords to insects protection from the sun and gives them resting-places, so that they can extend their normal flight indefinitely. It should be kept less than a foot high. On account of the wonderfully quick growth of tropical vegetation this was one of the principal items of expense in the Panama work. The clearing should be extended about 200 yards from villages and 100 yards from isolated dwellings. The individual farmer can get excellent results, at any rate, if he will clear off for 100 yards or so about his dwelling and screen the house. Vegetation at the edges of ponds and streams containing *Anopheles* larvæ should be cut short.

4. *To prevent access of mosquitoes to infected persons* before they reach the healthy.

(a) We screen our malarial patients in the hospitals or at their homes.

(b) We separate, as far as possible, the quarters of the native (and presumably infected) population from our own. This is easier said than done, as questions of convenience and economy naturally arise here. We do the best we can, however, and no doubt get noticeable results when able to carry out our plans.

5. *The effort to lower the susceptibility to malaria* of the persons we are trying to protect. We do this by what we call the prophylactic use of quinin. There has been a good deal of discussion pro and con as to the value of this procedure, but it was thought on the Isthmus to have considerable value, although it should not by any means be trusted to the exclusion of other methods. Prophylactic quinin has lately been found by experiment to reduce markedly the malarial index and the splenic index in affected regions. Celli, writing of the restriction of malaria in Italy, states that the district of the Roman Campagna has been brought back to civilization by the wholesale administration of "state quinin," aided by hydraulic reclamation of land. The dose is about 6 grains daily of the sulphate for the average-sized adult male. The main trouble in this connection is to get people to take the medicine. Old residents will ordinarily take it, but newcomers fight shy. In Panama it is kept on the mess tables, and a quinin dispenser goes daily among the workmen and offers it to them and tries to induce them to take the prophylactic. It was found a great help down there to make it in an alcoholic solution. On account of the alcohol many men will take the drug who otherwise would not do so.

A method supplementary to those described, and often of considerable value, especially in tents, where it is easy of application, is a systematic daily *destruction*, with an entomologist's chloroform bottle, or by the so-called "swatter," of *adult Anopheles mosquitoes* found resting on the walls, especially in dark corners. This is a useful addition to the work anywhere, but particularly in newly occupied localities where we have not yet had time to put the other methods in successful operation. The "swatter," or "slapper," is a piece of wire gauze six inches square attached to a two-foot stick. If the building or tent is not screened this is used four or five times a day; if screened it is used morning and evening. It is advisable to have dwellings well lighted and the walls a light color or whitewashed, or to use some portable illumination. In screened buildings one may also add mosquito traps.

Giemsa at the Khartoum Quarantine Station destroys adults by spraying with the following mixture:

Pyrethrum tincture . . . . .	580 gms.
Potassium soap of commerce (as far as possible odorless) . . .	180 "
Glycerin . . . . .	240 "

Before using mix with twenty times its volume of water. Spray about rooms with a special pump; use a hand pump in small rooms. Apply once a week. It is best to work down the wind.

A method often used in practice in antimosquito work, and not mentioned in the Carter classification, is to obtain the passage of sanitary codes or local laws, providing penalties for individual owners allowing mosquito-breeding conditions on their premises. This is naturally a "two-edged sword," but, handled with discretion, often enables the worker to attain results he would not otherwise have achieved.

Bentley, in Bengal, has a broader outlook on the question of the prevention of malaria. He says a paramount influence is exerted (*e. g.*, in England and Holland) by advancing civilization, especially the extension of agriculture and the improvements in agricultural methods. Malaria, formerly quite extensively present in England, is now entirely unknown. This desirable result is apparently due to the fact that in that country agriculture, with its concomitants of clearing and drainage, has practically covered the whole island, thus gradually but thoroughly removing all breeding places. This result would in the course of time naturally follow in all civilized countries. For some generations in America, and longer in now unsettled tropical countries, we must, however, fight malaria along the lines we have indicated above.

General Gorgas, the originator and demonstrator of many of the methods described, would no doubt be one of the last to abandon them in actual practice. He has, however, finally conceived the original and very interesting idea that adequate sanitation is in

the last analysis a resultant of sociological factors rather than scientific ones; that the amelioration of living conditions that would result from the abolishment of poverty must be the final answer to all problems arising from bad sanitation. He thinks that the most promising outlook for the removal of indigence would be afforded by the institution of the "single tax" method of taxing land. No doubt we had better try this remedy for the relief of poverty before experimenting too extensively with the birth-control formula of the Neo-Malthusians. However, that is another story and is outside the province of our paper.

The above completes a brief but comprehensive view of the measures used in antimalarial campaigns. I should like to emphasize again that I think drainage and filling in are the vitally important things. The use of them alone controlled the situation in Havana according to Le Prince.

Before leaving this part of the subject I wish to recall to the reader a brilliant piece of work accomplished by Ross at Ismailia in Egypt. This is one of the stations of the Suez Canal Company. Originally healthful, the result of improvements and irrigation was to leave shallow ponds and marshy areas about the town. Malaria developed, and out of a population of about 10,000 there were probably 2500 cases of the disease in a year. The place was practically ruined. Ross went there about 1902 and inaugurated the antimosquito work; in a year the cases had dropped to about one-tenth, in three or four years there were no fresh cases, and no malaria was contracted there at all. In a general way he used the same methods I have described, especially filling in and draining. His final results look better than ours on the Isthmus. The reason is, no doubt, that he had a limited area to deal with in his experiment, not so large a population, with no excavation going on, and absolute control of the situation. We had over 40,000 employees distributed over a line forty miles long, to say nothing of the natives living contiguously, and with the whole face of nature changing nearly every day, owing to the active engineering work in progress. The difference can be readily appreciated. Our results are necessarily not perfect, but they are satisfactory, and, on the whole, a wonderful success.

A word as to the *cost* of the antimalarial work. I shall not embarrass the reader with any figures as to the number of millions of dollars expended by the Sanitary Department on the Isthmus in this work since the beginning. This would burden the memory unnecessarily. Moreover, the figures, stated in this way, look big and encourage the enemies of sanitation. Strange that there should be any at this stage of the world's history, is it not? It may be stated that the expenditure for sanitation was about \$3.50 annually, or say approximately one cent per day, for each individual in the total territory covered by the work, a population of about 100,000.

Of this \$3.50 about \$2.00 was spent on the antimosquito work. A ridiculously small price to pay for the results obtained, as anyone should see; and yet there are people who complain of the cost of sanitation.

THE PREVENTION OF MALARIA IN WAR. We are extremely likely to be called upon to give advice in this connection in the present emergency. Along what lines should it be? First and foremost, *preparation for the expedition*. Melville says truly that the only serious problem in a *tropical* campaign is disease, and that mainly malaria. He continues:<sup>8</sup> "Now there is this difference between a human enemy and disease. The former may alter his plans at the last moment and our plans may have to be changed accordingly. But disease does not alter its laws. As far as we know or can guess at those laws we are able to calculate confidently on their regularity, and our plans can be fixed accordingly. It is almost a platitude to say that the success of any tropical campaign is settled as much in Whitehall as on the actual spot. An ill-provided, ill-thought-out expedition can only end in disaster, however brave the soldier, and however skilled his commander. What is necessary is that the objective should be clear, the means exactly proportioned to the end, and all things necessary provided before the start is made." Careful consideration should be made of the conditions likely to be met and such plans laid down beforehand as are most likely to lead to success in the warding off of disease, even perhaps to the extent of influencing the selection of lines of advance and season of beginning. If at all practicable the men forming an expeditionary force should be picked, strong and healthy men, not too young, and, if possible to determine, free from malarial infection at the start.

Camp sites should be selected with reference to the possible prevalence of conditions favorable to malaria. Melville advocates the construction and sending out of portable mosquito houses with troops going to notoriously malarial localities. This is perhaps a counsel of perfection. We should at least have mosquito nets, head nets, and gloves, and the men instructed as to the importance of using them. Not all of the conditions just mentioned will apply, of course, to our present expeditions over-seas. However, it is well to bear them in mind, and give them such consideration as is possible under the circumstances. In other words the question of the malarial factor should not be entirely disregarded even in the present projected campaign in temperate latitudes.

When once in permanent camp, such measures as are practicable along the lines we have been considering should be undertaken in regard to the breeding places of mosquitoes. Some of them must of course be modified to correspond to local and temporary conditions. The general principles of action, however, remain the same.

<sup>8</sup> Ross, Ronald: *The Prevention of Malaria*, New York, 1910, p. 587.

In camping the proximity of native villages should be shunned. We avoid fatigue as much as possible and give prophylactic quinin; we give 6 grains daily, or 15 grains on two consecutive days of the week, the last method being perhaps better for soldiers, as it causes less complications in the administration of the prophylactic.

Essential oils, such as oil of pennyroyal or oil of citronella, when applied to the face and hands, have considerable influence in keeping away mosquitoes. Of course, the protection so afforded is not absolute, but is only a help to other more important methods. Kerosene similarly applied has some protective effect. The main trouble with these is the quick evaporation. Punkas or individual palm-leaf fans afford some aid; also electric fans, when available.

TROOPS UNDER PEACE CONDITIONS. Malaria in our Army today is not over one-tenth what it was a generation ago. I am speaking of peace conditions such as apply in posts and cantonments, the latter being in effect rather a sort of crudely constructed posts than camps.

Naturally, measures of prevention should be about the same as I have described for the civil population. We had better extend our *clearing and drainage* operations, however, beyond the limits recommended for temporary occupation. Major Fowler, of the Royal Army Medical Corps, says we should go for 2000 yards beyond the barracks in the tropics and subtropics. Ordinarily we would control, and could readily handle, this amount of ground at most of our army posts.

The *segregation* of the soldiers from the natives is a matter of considerable importance, though of course a difficult if not impossible thing to effect. Still, we must do the best we can along this line. Of course, if our clientele are going out to pick up infection from unprotected places our elaborate precautions at home are often made of no avail. I suspect that Craig got a lot of his malaria at Stotsenberg in this way rather than from infected insects flying in from the distance of a mile or two from the post. Frequenting native houses at night, a favorite occupation of the soldier, is certainly an ideal method of contracting malaria, as well perhaps as other diseases. I mean this factor is an added danger in soldiers, more important than the same thing in civilian communities.

When the conditions are very bad, *prophylactic quinin* should be given to the soldiers, also to the natives where these are, as we often find them, under our control.

When the population is not too large, and time and opportunity allow, the method of procedure recommended by Vedder,<sup>9</sup> and aimed at the reduction by treatment of the number of infected human beings, may be tried. It is as follows:

<sup>9</sup> Vedder, Edward B.: Sanitation for Medical Officers, Philadelphia, 1917.

1. Early notification of all cases of malaria, following these up with malarial register cards.

2. A survey of the population to detect "carriers."

3. Efficient treatment of all cases, including carriers.

The minimum treatment recommended is quinin, grains xxx daily, until symptoms are gone and plasmodia cannot be found; then quinin, grains xv daily, for two weeks; then quinin, grains x daily, for two weeks; then quinin, grains vj daily, for at least two months.

Barracks and hospitals should be *screened*, especially the latter, as they are otherwise likely to form important foci of infection.

*Instruction* of the soldiers in the matter of the conveyance of disease by insects will perhaps afford some help, but like the venereal instruction, is not to be entirely relied on. Sanitary education of children in the schools is another matter and worthy of more exploitation than it has yet had.

CONCLUSION. The above is only an outline sketch, a rather lengthy one it is true, and on broad lines, of the protean phases of a big subject. If I shall have succeeded in impressing on the reader some idea of the great necessity of considering the importance of malaria among troops and in war, and in stimulating him to further reading and thought about it, my labors will not have been entirely in vain. Without some such suggestion the question might easily be neglected by the physician who has been practising in the more populated and cultivated districts of our temperate zone, where the malarial incidence has been so much reduced by natural causes, operating often so gradually, that one unconsciously loses his sense of proportion in relation to the potentialities of a formerly prevalent and damaging disease.

It might easily happen that it would count, and with disastrous effect, before the close of the present world war.

Let us then take note of this undesirable possibility now and employ in advance all the precautions that the enormous recent advances of sanitary science and its applications in contemporary practice have made available to us today.



## THE ROENTGENOLOGIC DIAGNOSIS OF PRIMARY CARCINOMA OF THE LUNG.\*

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PRIMARY carcinoma of the lungs and bronchi is a rare condition and one in which it has been very difficult to make a diagnosis clinically. The larger number of cases reported have been taken from postmortem data and many of them were incorrectly diagnosed or overlooked during life.

In the roentgenologic examination of the chest there is a group of findings associated with primary pulmonary carcinoma that up to this time have not been fully recognized and accorded their true worth. The roentgen examination may early point to a lesion in the chest, thus making it possible, except in the very early and atypical cases, to make a definite diagnosis of primary carcinoma of the lung.

From a brief review of the literature it appears that up to this time there have been 428 authentic case reports of primary carcinoma of the lung. The most complete and excellent monograph on the subject has been written by Adler,<sup>1</sup> who collected 374 definite cases and several others which, though questionable, bore sufficient evidence to cause him to put them in a doubtful column.

The pathology of primary pulmonary carcinoma is most interesting. The rarity of the disease is somewhat unusual since in the lungs and bronchi there is such a preponderance of tissue of epithelial structure. There are three types of epithelial cells: the columnar epithelium lining the bronchi and larger bronchioles, the flattened or cubical epithelium lining the alveolar spaces, and the glandular epithelium found in the mucous glands. The endothelial cells lining the pleura may also be mentioned as a possible source of primary carcinoma of the lung but will not be discussed in this paper. In most instances the carcinomas originate from the columnar cells lining the larger bronchi. The favorite site of origin is said to be in the second or third division of the main bronchus, but any portion may be first involved. The primary nodule enlarges, invades the bronchial wall and extends out into the smaller bronchi and into the parenchyma of the lung. The bronchial lymph glands are usually involved, but numerous cases are on record in which they showed no evidences of metastases, although both lungs were affected. There seems to be no established data in regard to the

\* From the division of Roentgenology, Mayo Clinic, Rochester, Minnesota. Presented for publication May 14, 1917.

frequency and the favorite sites of metastases outside the thoracic cavity, unless it be the axillary and cervical lymph glands. The liver is not often involved. Many cases have been reported in which there were no metastases, but at autopsy both lungs have been found extensively infiltrated with cancer cells. The brain may be mentioned as a probable, and at times the only, site of metastasis in primary lung carcinoma.

Grossly there are three types of primary carcinoma of the lungs and bronchi: The infiltrative, the miliary and the mixed types. The infiltrative type is reputed to be the most common. The condition starts in one of the larger bronchi as a nodular tumor of varying size. It penetrates the wall and invades the lung along the bronchi and bronchioles, the alveolar walls and air spaces by way of the bloodvessels and lymphatics, by direct extension, by gravity and by aspiration. A single lobe may be affected, usually the lower, or there may be massive areas involving parts of both lungs. In the miliary type the nodules are very numerous, two to ten or more times the size of macroscopic miliary tubercles; they have a more or less symmetrical and diffuse distribution throughout both lungs, and are found far out in the periphery as well as in the central parts. The pleura may be involved with carcinoma or with simple chronic inflammatory changes. The tumors are round in form, grayish white in color, invasive in character, not sharply demarked from the surrounding lung tissue, and firm on section. Several of them may coalesce to form larger irregular nodules. Degeneration and central necrosis sometimes occur, leading to caseation and cavity formation. The mixed type presents both the infiltrative and the miliary forms in the same case. In addition to a large and hard wedge-shaped or nodular area in one or more lobes, the remainder of the lung is diffusely studded with miliary nodules varying in size and number, depending on the duration of the disease.

The symptoms are variable and not diagnostic, though sometimes suggestive. The age incidence of the disease is similar to that of all malignancies. Males are more frequently affected. Cough is an early symptom; it is usually slight but constant and distressing. Expectoration, if any, is moderate in amount; it consists chiefly of mucus and at times may be blood-stained. Hemoptysis is common, but the quantity of blood is small. Inspiratory dyspnea comes on early, is nearly always present and is exaggerated by exertion. Hoarseness and change of voice from pressure-paresis of one or both vocal cords is common. Pain is a prominent, but not early, symptom. It is associated with substernal pressure symptoms or pleural involvement. Pressure may give rise to dysphagia. Weight loss and weakness are pronounced and progressive. A rise of temperature of  $0.5^{\circ}$  to  $1^{\circ}$  is usual; chills and sweats are rare. The infiltrative type runs a longer course than the miliary or mixed type.

The physical findings are such as would be expected in massive

or patchy infiltration and consolidation of the lung from any cause. Pleural effusion may mask these signs; on aspiration the fluid may be straw-colored, blood-stained, or darkly discolored. Engorgement of the veins of the anterior chest wall and edema of one or both arms may be present. Enlarged supraclavicular or axillary glands, are suggestive, and removal of such glands may aid the diagnosis.

In most instances the roentgen findings in primary carcinoma of the lungs are pathognomonic of the disease, and may be the first to suggest the exact nature of the pulmonary lesion. The areas of increased density, their size, shape, and position, are usually characteristic and aid in the clinical diagnosis more than most other signs. This does not imply that all other signs can be slighted or discarded, for it is by a careful collection and correlation of all the facts that a satisfactory differential diagnosis may best be established.

In the roentgen examination three types of the disease are recognizable: namely, the infiltrative, the miliary, and the mixed, which correspond to the gross pathological groupings. For convenience each type will be discussed separately though many characteristics are common to all. A striking feature in all types and one of considerable diagnostic importance is the absence of practically any increase in mediastinal density. The presence of extensive pleural involvement in primary carcinoma of the lung renders the interpretation of the roentgenogram correspondingly more difficult, but not impossible. The presence of large pleural effusions tends to completely mask the roentgenographic picture and to conceal the underlying and principal pathological condition in the lung. A second roentgen examination is necessary after thoracentesis. Fortunately these latter two conditions rarely occur until the terminal stages of the disease.

In the stereoscopic study of the infiltrative type of primary carcinoma of the lung, the roentgenogram shows one or more areas of increased density along the roots of the larger bronchi. The shadows are homogeneous or partially mottled. The borders are infiltrative and not sharply demarked. The areas of density are wedge-shaped, with the apex pointing toward the hilus, and there may be either unilateral or bilateral involvement. The degree of density is marked but varies with the extent and duration of the disease. Until there is extensive involvement the process does not reach the periphery of the lung, so that small areas of air-filled lung tissue may be seen between the growth and the chest wall. The most frequent site of this type of lesion is in one of the lower lobes. There is always present a hazy shadow-zone surrounding the growth, due to congestion from active hyperemia or passive congestion due to mild pressure, or to both conditions. The roentgen shadows found in this type of carcinoma of the lung at times makes the diagnosis difficult. The roentgenogram will show the presence of a lesion in the lung, but if the neoplasm is in an early stage the areas of

density may not be entirely typical of primary infiltrative malignancy. In such cases the roentgen diagnosis can be only tentative, and if the other findings are not sufficiently corroborative a subsequent roentgen examination should be made.

Two of the cases studied by us were of the infiltrative type. In one (Case 176118) the roentgenogram showed the presence of a lesion in the lower right lung, the exact nature of which was doubtful until an exploratory thoracotomy and a microscopic examination were made. In the other case the lesion was more extensive and typical of primary malignancy. Postmortem examination confirmed the diagnosis.

In the miliary type there are innumerable regular, irregular, or conglomerate small areas of increased density extending throughout all the lobes. Their borders are poorly defined and not sharply circumscribed from the surrounding parenchyma of the lung because of the marked infiltrating character of the neoplasm. The process is diffuse throughout both lungs and the areas of density are distributed as uniformly near the hilus as in the periphery of the lung. The shadows show no tendency to be arranged in groups or clusters. There are usually no true cavities but there may be localized dilatations of the smaller bronchi and bronchioles, the walls of which may be differentiated from cavity formation only by the stereoscope. Dilated bronchioles are recognized roentgenologically by the absence of any thickened wall. Two of the cases herein described are of the miliary type (Cases 159177 and 126018). In one the diagnosis was confirmed at autopsy; in the other no autopsy was made.

The mixed type of primary carcinoma of the lung includes a combination of the infiltrative and the miliary forms. In this type are found poorly circumscribed, homogeneous, or slightly mottled areas of increased density in one or more parts of the lung, and multiple smaller areas of increased density similar to those found in the miliary type, diffusely studding the entire remaining portions of both lungs. Two of the cases (Cases 160751 and 109685) were of this type. In both the diagnosis was confirmed by a post-mortem examination.

The differential diagnosis of primary carcinoma of the lung must be made from a large number of other pathological conditions found in the thorax, which in the roentgenogram may in a measure simulate carcinoma. A long and detailed description of each is unnecessary here, but the salient and important points concerning the more confusing conditions are as follows:

Bronchiectasis may be confused with the infiltrative type of primary pulmonary carcinoma in the early stages, or when either lesion is atypical. Moore<sup>2</sup> has shown, however, that in bronchiectasis the shadow is fan-shaped and extends to the periphery; also that when a lower lobe is involved the costophrenic angle is obliterated.

ated and the process is usually though not always bilateral. Further, in bronchiectasis, cavitation is invariably present, with shadows suggesting dense fibrosis around the cavity. When bronchiectasis is suspected the patient should be induced to attempt the evacuation of the contents of the cavity by forced coughing and expectoration, in order that the cavitation may be shown more clearly in the second roentgenogram.

Pulmonary abscess and encysted empyema are usually not difficult to differentiate from carcinoma. In such cases the areas of increased density are sharply circumscribed and surrounded by a shadow zone of inflammatory change beyond which is the normal healthy lung area. The presence of the shadows of a fluid level with a gas bubble above in an abscess cavity may be further aids. Finally, the shadow of a thickened pleura is more frequently associated with these conditions than with pulmonary malignancy.

In lobar pneumonia the shadows are usually localized, soft and hazy, and vary in density with the stage of the disease. In the early stage there may be only a slight difference in density from the surrounding lung tissue, while in the later stages the density is greater and the shadow is sometimes mottled. Any part of the lung may be involved but the condition usually includes practically an entire lobe. The pleura is much more frequently involved. Clinically, of course, the differentiation is even more emphatic.

Regarding syphilis of the lung very little is known definitely from the clinical stand-point and less from the roentgen stand-point. While the disease seems to be more common than formerly and is recognized clinically, Dr. W. W. Bissell informs us that he has never seen a case in 4000 postmortems. In one proved case in the Clinic the roentgen examination revealed marked enlargement of the mediastinal shadow with areas of increased density in the regions of the main bronchi while the periphery was free. The heart shadow was greatly enlarged and the aorta dilated. At autopsy multiple diffuse areas of dense patchy fibrous infiltration were found in both lungs near the hilus, together with a large heart showing marked myocardial changes and a saccular aneurysm of the ascending aorta. We have never seen or at least have never diagnosed gumma in the parenchyma of the lung. Gumma in the mediastinum may be differentiated from primary carcinoma of the lung. The shadow is usually large, well circumscribed, homogeneous, and unilateral or bulging to one side.

In primary sarcoma and lymphosarcoma of the lung the roentgenogram corresponds in its characteristics to that of mediastinal gumma, except that in sarcoma the tumor shadow tends to be larger. Infiltration and involvement of distant portions of the lung rarely occur.

In Hodgkin's disease the roentgenogram usually shows areas of increased density which are symmetrical, bilateral, well circum-

scribed and limited to the mediastinum. There are no changes in density along the course of the main bronchi unless the tumors are very massive or there is marked myocardial degeneration leading to much passive congestion.

In actinomyces and allied affections of the lung the roentgen findings may be differentiated from those of primary malignancy. The areas of increased density are "stringy" and fan-shaped in arrangement, usually found in the periphery and surrounded by a soft shadow zone of inflammatory reaction. The pleura is involved early and there may be an area of increased density corresponding to a tumor on the bony chest wall.

There is a marked difference in the roentgen shadows found in primary and metastatic malignant disease of the lungs. As in the metastatic carcinomas, sarcomas, and mixed tumors the roentgenogram shows the same characteristics and their roentgen appearances may be enumerated collectively. According to Moore<sup>3</sup> and one of us (Carman) the areas of density in metastatic malignancy of the lung are rounded, regular, clearly circumscribed, soft and homogeneous. They do not show a shadow zone of inflammatory reaction surrounding them; they vary in size, are usually multiple, and may occur in any part of the lungs.

Cysts of the lung show in the roentgenogram as large, clearly circumscribed and homogeneous areas of increased density. They are usually single and are found in the right lower lobe.

Fibromyxoma of the lung is easily differentiated from primary carcinoma. In the former the area of increased density is large, massive, homogeneous, and well circumscribed. An entire lobe is usually involved, most commonly the upper. Since the tumor is slow-growing there is very little, if any, congestion-shadow surrounding it.

The differentiation from the roentgenogram of pulmonary tuberculosis will seldom be difficult. In chronic pulmonary tuberculosis the periphery is the common location of the areas of increased density, with very few, if any, changes in the hilus. The shadows are more circumscribed. The upper lobes, especially the apices, are usually the first and most commonly involved. Cavitation may be present, and there is frequently an associated pleuritis. In acute or subacute miliary tuberculosis the individual areas of increased density are smaller, more regular in shape, more discrete, more uniform in size, and with greater peripheral involvement than in the miliary type of carcinoma.

Pneumokoniosis produces symmetrical "stringy" shadows distributed along and near the main bronchi. They never extend to the periphery. In the mediastinum enlarged calcified bronchial lymph glands are present and show as clear-cut, rounded, and circumscribed areas of increased density.

Chronic passive congestion also produces symmetrical "stringy,"

diffuse shadows. In the hilus there are large, symmetrical areas of increased density. The heart shadow is usually enlarged in both lateral directions, and fluid may be present.

In simple chronic pleuritis stereoscopic examination shows that the area of increased density is located on the surface of the lung. If located at the base of the lung the costophrenic angle may be obliterated and the areas of density limited by an oblique line.

In transudates and exudates into the pleural cavity the area of density is small or large and homogeneous. It may present a fluid level that changes with position. Such conditions are usually located at the base and there is an obliteration of the costophrenic angle. The condition may be bilateral. The heart shadow may be enlarged, because of cardiac decompensation and dilatation, and the heart may be displaced.

Bronchoscopy is to be mentioned for completeness. It is a somewhat formidable procedure and usually impracticable except in the hands of the most expert. Even then it may be disappointing. Negative findings from the bronchoscopic examination should not be regarded as final. Exploratory thoracotomy should be considered in early, doubtful, and borderline cases, or when the patient's symptoms indicate the necessity of surgical interference.

The following are the histories of 5 cases of primary pulmonary carcinoma:

CASE 176118.—A male, aged thirty-five years, miner, registered in the Clinic October 24, 1916. The family history was negative for tuberculosis, cancer, and lues. The patient had had pneumonia thirteen years before with the subsequent expectoration of one-half a tea-cup of purulent material supposedly from a small abscess in the right lung. Since then he had had good health. For the past eight months he had complained of continuous dull ache in the right lower chest with some cough and expectoration. No fever or chills. Weight loss, 16 pounds. Some dyspnea for years, but more marked in past eight months, and growing worse. Hemoptysis two months before but only slight, probably 3 or 4 drams. No gastro-intestinal or urinary symptoms.

The physical examination showed considerable emaciation and some dyspnea on exertion. There was a large area of dulness, increased fremitus on exertion, and diminished breath sounds below the angle of the right scapula. The systolic blood-pressure was 95; the diastolic, 72; the pulse, 76; and the temperature, 98.2°. The urinalysis was negative. The sputum examinations were negative for tubercle bacilli. One blood Wassermann was negative.

In the roentgenogram could be seen a mottled area of increased density involving the lower right lobe and the base of the middle right lobe and extending outward along the bronchi, though not to the periphery. The shadows were centrally placed; probably primary infiltrative carcinoma. There were multiple small areas

of increased density and in the lower left lobe, probably anthracosis (Fig. 1).

A clinical diagnosis was made of a probable chronic intrapulmonary lesion at the base of the right lung.

Operation; exploratory thoracotomy. Three inches of the seventh and eighth ribs were resected on the right side in the posterior axillary line. The pleura was  $\frac{1}{8}$  inch thick. The lung tissue was hard, tough and coal-black, and for a finger's length had the same firm consistency throughout, and bled easily. Specimens of the pleura and the lung were removed for microscopic diagnosis.

The pathological diagnosis was primary pulmonary carcinoma.

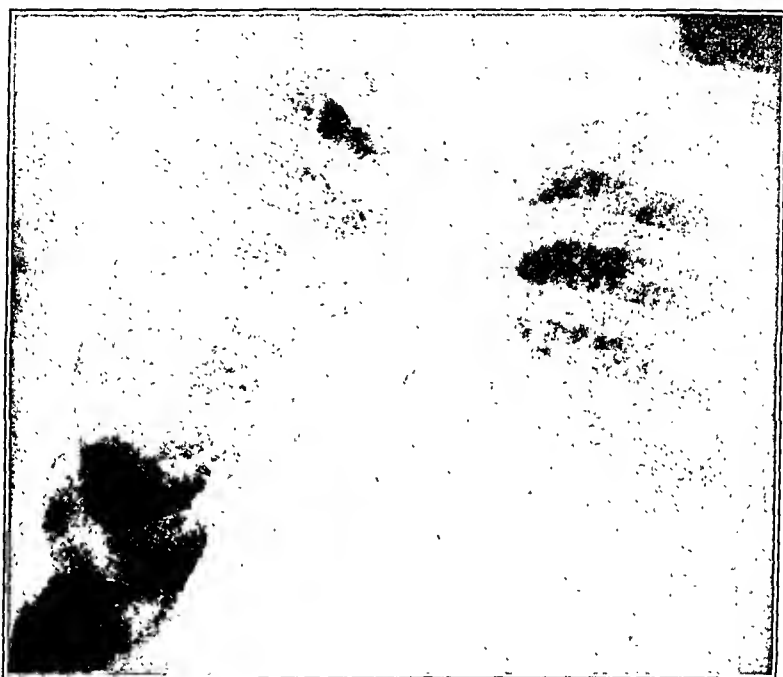


FIG. 1

CASE 159177.—A female, aged forty-seven years, registered at the Clinic May 8, 1916. The patient's father and one son died of tuberculosis. One year previously she began to complain of weakness and dyspnea and was treated for hypertension. The loss of strength and the dyspnea had increased markedly during the past seven months and in addition she had a chronic irritative and non-productive cough. There had been no chills, fever, or sweats. She did not sleep well and had lost 25 pounds in weight in the past year. No pain; no gastro-intestinal, urinary, or cardiac symptoms.

The physical examination showed moderate emaciation and pallor. There were signs of moderate dullness at the bases of the lungs, crackling coarse rales, exaggerated breath sounds, and prolonged expiration. The average systolic blood-pressure was 140; the average diastolic, 98; pulse rate, 90; temperature, normal. The



vocal cords were negative. The urinalysis was negative. Hemoglobin 83 per cent. Sputum negative for tubercle bacilli and carcinoma cells.

In the roentgen examination, multiple diffuse areas of increased density were found throughout both lungs. The condition was believed to be primary carcinoma of the miliary type (Fig. 2).

The clinical diagnosis was primary carcinoma of the lungs.

Autopsy revealed primary carcinoma of the lungs with no evidence of metastases in the lymph glands, liver, gastro-intestinal or genito-urinary organs, and no evidence of any other primary growth.



FIG 2

CASE 126018.—A female, aged seventy-one years, registered at the Clinic March 8, 1915. One brother had died of malignant disease. Patient's menstrual history negative; menopause thirty years previously. Complaint: Small, hard, painful multiple tumors in the left side of the neck which had been noticed ten months before for the first time. The nodules had gradually enlarged until three months previously. There was some pain down the left arm and soreness in the left shoulder. Considerable dyspnea noted during this time. No choking sensations, dysphagia or genito-urinary symptoms. No gastro-intestinal symptoms except slight loss of appetite during the past five or six months. Patient had lost 20 pounds in weight and considerable strength.

In the physical examination many enlarged, hard, tender glands

were found in the left cervical region. There were signs of multiple ill-defined areas of consolidation throughout both lungs. Urinalysis, Wassermann test and sputum examination negative.

The roentgenogram showed multiple non-circumscribed areas of increased density throughout both lungs with equal distribution in the bases and the apices. Roentgen diagnosis, primary carcinoma of the mixed type (Fig. 3).

The clinical diagnosis was carcinoma of the lungs with metastases to the left cervical glands. The patient died at her home May 23, 1915. No autopsy.



FIG 3

CASE 109685.—A male, farmer, aged fifty-seven years, registered at the Clinic July 4, 1914. His family history and previous history were negative. He denied venereal infection. The patient had dyspnea on slight exertion and loss of strength which had been increasing gradually over a period of four months. Slight cough; no expectoration, hemoptysis, night-sweats or chills. His family physician wrote that his temperature had not been elevated and at times was subnormal. The patient complained of sleeplessness on account of cough, and of being unable to lie in a recumbent position. Up to the time of admission there was no history of edema or cardiac decompensation.

The physical examination showed the blood-pressure to be 118-78; pulse, 90; temperature, 98.2°. The patient was well developed but slightly undernourished. His complexion was ashen, with cyanosis exaggerated by slight muscular exertion. There were signs of con-

solidation in patches on both the anterior and posterior sides throughout both lungs, with numerous generalized moist crackling and wheezing rales, which, however, were more marked over the right lung. The heart sounds were good; no murmurs. There was a slight mucopurulent discharge from the nares, more marked on the left side. Slight simple rhinitis and pharyngitis. Antra negative. Urinalysis negative. Hemoglobin, 86 per cent. White blood cells, 9000. Sputum examinations were negative for tubercle bacilli and cancer cells.

The roentgen examination showed multiple areas of increased density throughout both lungs, with massive areas situated in the base of the upper left and the middle right lobe. The roentgen diagnosis was primary carcinoma of the mixed type (Fig. 4).



FIG. 4

The patient was treated symptomatically for eight weeks. The dyspnea increased and his strength diminished. During this time the myocardium showed marked decompensation. The pain in the chest was not pronounced. He developed symptoms of myocardial insufficiency, fluid in the chest, edema of the lower extremities, and the usual constitutional symptoms resulting from a chronic intoxication. Death occurred September 3, 1914, six months after the onset of the condition.

The clinical diagnosis was primary carcinoma of the lungs.

The autopsy (two months after the roentgen examination) revealed 400 c.c. of blood-stained fluid in the left pleural cavity.

The surfaces of both lungs had an irregular nodular appearance and there was extensive chronic pleuritis and pleuropericarditis. On section the lungs showed multiple diffuse grayish-white nodules of regular and irregular shape, varying in size up to 2 cm. These were hard, resisted cutting and showed no tendency to central necrosis. They were distributed around the larger bronchi and bronchioles and in the lung parenchyma. They were infiltrative rather than encapsulated and not sharply demarked from the surrounding lung structures. The lower half of the upper right lobe and the base of the upper left lobe were almost completely occupied by hard massive tumors presenting on section the shape of wedges with the apex pointing toward the hilus, to which they apparently extend. The bronchial and other lymph glands were not involved. There were no evidences of tumor, either primary or secondary, in any other parts of the body (Fig. 5).

The final diagnosis was mixed type of primary pulmonary carcinoma, having its origin in the bronchial epithelium.

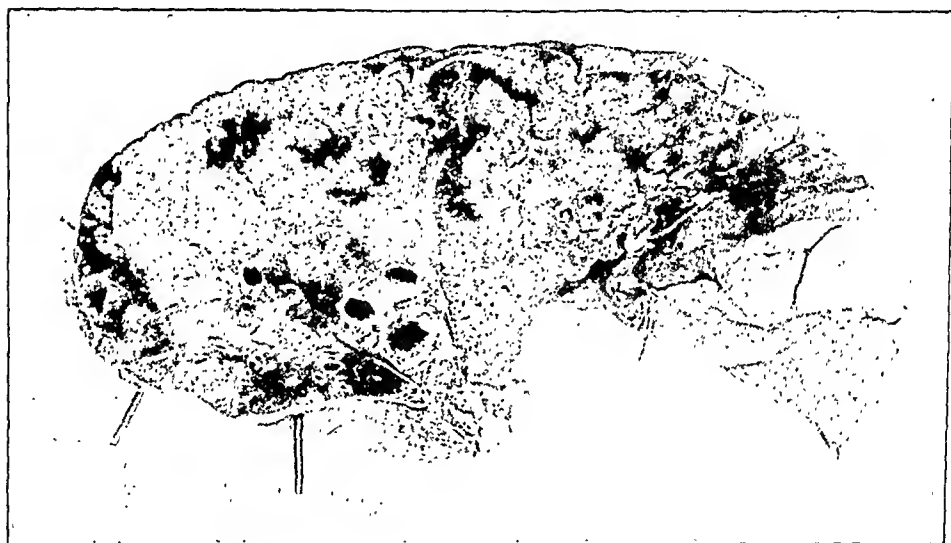


FIG. 5

CASE 160751.—A male, aged sixty-one years, registered at the Clinic May 26, 1916. His mother died of carcinoma of the breast at sixty-seven. He had been married thirty years; his wife and two children were living and well. For the past six months he had had gradual loss of weight and strength; with it a slight hoarseness and change in the voice; no unilateral sweats. During the same period of time he had had a dry, hacking cough; no hemoptysis. He had noticed bluish discoloration and distention of the superficial veins of the right forearm and hand. There was no edema of the right hand and no pain. A physician had stated that the right axillary gland was slightly enlarged, and had advised dissection of the axillary glands for fear of malignancy. A partial excision of the

right axillary lymphatics had been performed elsewhere in March, 1916, and the glands pronounced "not malignant." No gastrointestinal or genito-urinary symptoms. There had been a loss of 25 pounds in weight in six months.

The physical examination showed considerable emaciation and slight cyanosis of the lips and hands. In the right pectoral fold there was a recent operative scar of an incision that had healed by primary union. The larynx and cords were negative. Soft myocardial heart tones; rhythm of beat regular; rate, 100. There was moderate diffuse dulness throughout both lungs and poor expansion. The voice sounds were exaggerated. Prolonged expiration and crackling moist rales could be heard diffusely throughout the chest.



FIG. 6

Respiration, 26. Abdominal, genito-urinary, rectal, and urinary findings negative. Hemoglobin, 76 per cent.; white blood cells, 10,800. Wassermann negative. Sputum examination negative for tubercle bacilli.

The roentgenogram showed multiple areas of increased density extending throughout both lungs, with a massive area involving the base of the upper right lobe. The roentgen diagnosis was primary carcinoma of the mixed type (Fig. 6).

The clinical diagnosis was primary carcinoma of the lungs.

At autopsy, July, 1915, the examination of the thorax was limited. Both lungs and bronchial lymph glands were found to be extensively involved with carcinoma.

CONCLUSIONS.—1. There are three main types of primary carcinoma of the lungs which present characteristic gross pathological appearances: the infiltrative, the miliary, and the mixed.

2. The roentgen examination and the stereoscopic study of roentgenograms will early point to a pulmonary lesion and its probable nature.

3. The areas of increased density found in primary pulmonary carcinoma are usually quite typical, and can be differentiated from areas of increased density caused by other diseases in the thorax, including inflammatory changes and neoplasms, both primary and metastatic.

4. A careful correlation of the roentgen findings with the clinical history and the physical and laboratory findings usually makes a clinical and differential diagnosis possible.

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## A STUDY OF SIXTY-TWO CASES OF DIABETES OF FIFTEEN OR MORE YEARS' DURATION.

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IN 1912 among the 394 cases of diabetes traced out of 505 cases seen 17 per cent. had lived ten years or more, and if the large number of living patients who had acquired their diabetes less than ten years previously was subtracted the percentage of patients living ten or more years rose to 26 per cent. Now that five years have elapsed it has seemed desirable to again review our series of cases, but this time to discuss those patients who have survived their diabetes not alone ten but rather fifteen years. A sufficiently large number of such patients are available to make this investigation worth while, for the list contains 62 individuals. This number constitutes 6 per cent. of the total cases of diabetes traced up to the present time, but if we deduct from it those living cases whose onset occurred more recently than fifteen years ago the percentage of diabetics who have survived fifteen or more years from the onset of the disease rises to 11 per cent.

The duration of life of diabetics, however, is by no means limited to fifteen years, for among the 62 cases here discussed 37 are still

alive, and the average length of life for the total 62 cases up to December 1, 1916, was nineteen years and seven months. In the two following diagrams the duration of life of the living cases up to December 1, 1917, and of the fatal cases has been arranged according to the decade of age at onset.

These tables show that prolonged diabetes in the young is exceedingly rare. Indeed, there is only one case whose age at onset was less than ten years. This is Case No. 887, who showed at autopsy, according to Dr. J. E. Ash, a congenital deficiency of the pancreas. In the second decade there are 2 cases, one living and one dead. Case No. 1153, who is living, is one for whom many might challenge a diagnosis of diabetes, but although he has been many months at a time without having sugar demonstrated in the urine, glycosuria occurs whenever the diet is broken. Reference to this case will be made later, because this exceptional patient failed to show obesity.

Males constituted 55 per cent. of the 62 cases, and this proportion is nearly as high as that for the total cases of our series (60 per cent.). It is certainly an interesting fact that more males are treated for diabetes according to the diabetic authors, but that according to national statistics more women succumb to the disease.

The discovery of the disease was made quite independently of the appearance of symptoms in 17 of the cases. Thus, 12 patients, or 19 per cent., learned of their condition at examination for life insurance and 5 others upon the occasion of a periodic medical examination. The importance of life insurance examinations in this series becomes evident when one compares its incidence among these fifteen-year cases of 19 per cent. with the 6 per cent. incidence of insurance among the entire number of our cases available for this purpose; thus among the fifteen-year cases those discovering the disease by insurance were three times as frequent as was the rule for the total number of diabetics.

The predisposing factors in the etiology were few. Obesity heads the list, for it was present in 60 out of 62 cases; an hereditary or familial tendency existed in 21, or 34 per cent., in contrast to 21 per cent. for all of our cases; worry obviously existed in 9 and trauma also in 9, dietary excesses in the form of sweets in 8 and lues in 4. Two were cases of pregnancy and 8 of the patients obviously had gall-stones.

Obesity, here as elsewhere in diabetes, far outranks all other etiological factors. All the women were obese and all but two of the men. In one of these two exceptional cases the onset was at eighteen years of age. The patient (Case No. 1153) had been a very sickly child, with frequent attacks of cyclic vomiting. The other patient, Case No. 1060, was an hereditary case of diabetes, and later developed tuberculosis and nephritis. The importance of obesity was also recognized in the paper upon the cases of ten years' duration, and, in fact, 26 of the 67 patients then studied had weighed, at

some time or other, over 200 pounds. The more carefully our records are gathered the more frequently is obesity proved to precede the onset of diabetes. Naunyn makes the same remark regarding heredity. The degree of obesity which occurred in these 62 diabetics is graphically shown in the accompanying chart.

TABLE I.—FATAL CASES OF DIABETES OF FIFTEEN OR MORE YEARS' DURATION ARRANGED ACCORDING TO DECADE OF ONSET.  
DURATION IN YEARS.

AGE AT ONSET	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	TOTALS
61-70		1	1				1															3
51-60	2	1		1	1	3																8
41-50	1	3	2		1	1					1											9
31-40			1					1														2
21-30																				1		1
11-20							1															1
0-10																1						1
TOTALS	3	5	4	1	2	4	2	1			1					1					1	25

A familial or hereditary history of diabetes was obtained in 21, or 34 per cent., of these fifteen-year cases. This should be compared with the incidence of heredity, amounting to 25 per cent., in the ten-year group of our cases and the 27 per cent. of heredity which exists among those of Jewish extraction.

TABLE II.—LIVING CASES OF DIABETES OF FIFTEEN OR MORE YEARS DURATION ARRANGED ACCORDING TO DECADE OF ONSET.  
DURATION IN YEARS.

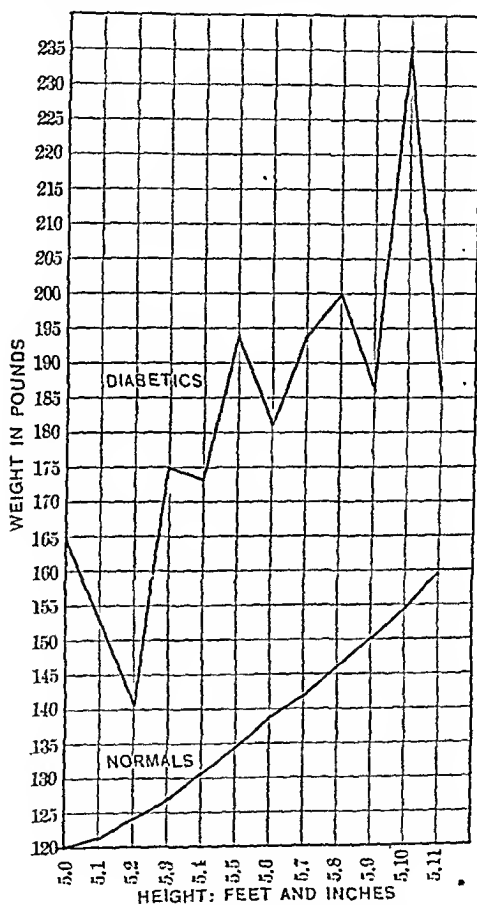
AGE AT ONSET	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	TOTALS
61-70						2																2
51-60	1	1		1	2			1			1											7
41-50	1	2		3	1	2		1				1										11
31-40		3	2	1	1	1	1	1						1				1				12
21-30			2	1	1																	4
11-20				1																		1
0-10																						0
TOTALS	2	6	4	7	5	5	1	3			1	1		1				1				37

The evidence here furnished therefore shows that among cases of diabetes of fifteen years' duration an hereditary and familial history of diabetes reaches its highest mark, but conversely and contrary to our present belief the presence of heredity may not be a favorable prognostic sign, because among our 251 hereditary cases of diabetes only 21, or 8 per cent., lived fifteen years.



Two fifteen-year patients (Cases Nos. 37 and 155) have children with diabetes. One of these children developed the disease at the age of nine years, which was eight years after the onset of the disease in his mother, and today, nine years later, is in good condition and free from sugar. The diabetes in Case No. 37 was of seventeen years' duration and began at the age of forty-five. This was twenty-

CHART I.—DIABETES OF FIFTEEN YEARS' DURATION. A COMPARISON OF THE WEIGHTS OF NORMAL INDIVIDUALS AND OF SIXTY-TWO DIABETIC PATIENTS PRIOR TO THE ONSET OF THE DISEASE.



one years after the birth of her son, who later developed diabetes at the age of forty-one years. It is also interesting that the wife of one of the fifteen-year cases had diabetes prior to its discovery in her husband, and this may account for the fact that he was treated so soon after the onset of the disease.

Trauma as an exciting factor in the onset of the disease among 9 of these patients is cited, but it is too indefinite to warrant conclu-

sions as to its importance, either pro or con. In only 8 of the cases was the overeating of sweets definitely noted. If the records were more complete in this regard the number of such instances might be greater. Smokers should derive consolation and smokers' wives should take warning when they learn that more than once we have been told by men that, following the substitution of candy for tobacco at the solicitation of their wives, weight increased and diabetes developed.

Few cases in our entire series have shown sufficient trouble with the liver to make this a serious factor. There have been three deaths from cirrhosis, and one of these occurred in a fifteen-year patient. About half (29) of the 62 fifteen-year cases presented a palpable liver, but this was usually attributed to the ease of palpation because of emaciation rather than to any demonstrable enlargement of the liver.

The knee-jerks were present in all cases, and in only one were they even noted as diminished. It so happens that this case was the only one who showed an enlarged thyroid. In but a single case did the pupils fail to react. Of course, all of the cases have not been personally examined throughout the entire period of fifteen or more years, but this has been true of a large proportion. The normal pupils, in conjunction with the normal patella reflexes, lend very little support to the idea that long-lasting diabetes leads to the so-called diabetic tabes or that syphilis is common in diabetes.

Cataract was recorded in but 3 cases.

The teeth were noted as good in 19 out of 43 cases. Bad teeth do not necessarily precede diabetes, and by no means necessarily occur during its course, even if the disease is of prolonged duration.

The evidences of arteriosclerosis were numerous. Thus 36 patients showed distinct manifestations, and in only 14 of the 62 cases did we feel confident that the bloodvessels were normal. Gangrene occurred in 9 of the patients, and of these 5 have died. The records of the blood-pressure are meager, due in large measure to the early period at which many of the patients were seen. The systolic blood-pressure exceeded 190 mm. Hg. in 6 cases, ranged between 150 and 190 in a like number, and between 120 and 150 mm. Hg. in 9.

Nephritis was of common occurrence. During this last year special study was made of the renal efficiency of a few of the cases by our fellow-worker, Richard Ohler. He determined the non-protein nitrogen in 10 patients. In one-half of these it was less than 31 mgm., and was thus in harmony with the blood-pressures of this group, which were normal. In the other 5 cases 2 showed 50 mgm., one 40 mgm., and the other two 34 mgm. non-protein nitrogen per 100 c.c. blood. These 5 cases presented other characteristic evidences of extreme nephritis as well, although, strangely enough, all are now living. One, however, is at present in a very

critical condition, due to nephritis. To determine the degree of renal involvement in 2 cases, phenolsulphonaphthalein was injected, and the amount excreted in two hours was found to be about 30 per cent.

The fifteen-year cases now living diet more carefully and keep more nearly sugar-free than did those who have died. Of the 37 living cases, 13 very easily became sugar-free, and 11 of these so remain with slight or moderately restricted diet. One case, a pregnancy case (Case No. 309), is even able to eat pure sugar. With rather more restriction 4 cases became sugar-free, but in 3 other cases temporary fasting was employed to attain this end. Five cases became sugar-free with difficulty even with fasting and a very restricted diet. At present a diabetic diet has been abandoned by 2 cases, and 3 patients are obliged to diet very strictly. Nine of the fatal cases were never sugar-free from the time of the first visit until death, but 5 cases were known to be sugar-free at the time of death. Another became free after living five years on a moderately restricted diet. One case became sugar-free easily in four days; 1 after an operation (amputation); 1 after two weeks of moderately restricted diet; 1, who showed renal involvement, after six months of strict diet; 1 after nine months of strict diet with fasting days. In 3 cases it is unknown as to whether the patients were ever sugar-free. One of the fifteen-year cases did not become so until three years before death. There were but 5 of the 62 cases who entirely disregarded treatment, and of these 3 are dead. Among the ten-year cases of 1912 it was recognized that 55 of the 67 had received distinctly better treatment than the average diabetic patient.

In order to determine the quantity of protein per day which the patients were accustomed to eat, analyses of nitrogen in the twenty-four-hour amounts of urine of 19 cases were made. Six of these patients are now dead. Two of these fatal cases, when first seen, had a urinary nitrogen output above 21 gms. The urinary nitrogen of the remaining 4 varied between 13.8 gms. and 15 gms. These are high urinary nitrogens for elderly individuals. Among the 13 cases who are now living but a single one was found who showed as high as 21.5 gms. of urinary nitrogen. The only patients with urinary nitrogens less than 10 gms. are those patients who have been in the hospital on a very low diet. One of these is a patient who had been practically sugar-free for a year. Her nitrogen falls as low as 6 gms. The conclusion can be safely drawn that the protein in the diets of these cases of diabetes living fifteen or more years was usually not far from 75 gms., and the statement is also probably warranted that these patients had never lived long on a high protein-fat diet.

Blood-sugar determinations were carried out in 17 of this series of 62 cases. The results are shown in the following table:

TABLE III.—THE BLOOD SUGAR IN CASES OF DIABETES OF FIFTEEN YEARS' DURATION.

Case No.	Blood sugar, per cent.	Case No.	Blood sugar, per cent.
18 . . . . .	0.69	919 . . . . .	0.22-0.27
29 . . . . .	0.10	979 . . . . .	0.17-0.24
127 . . . . .	0.22	1007 . . . . .	0.09-0.23
155 . . . . .	0.29	1022 . . . . .	0.15-0.20
177 . . . . .	0.25	1043 . . . . .	0.19
352 . . . . .	0.14-0.27	1106 . . . . .	0.13
435 . . . . .	0.13	1111 . . . . .	0.18
887 . . . . .	0.15-0.43	1167 . . . . .	0.23
904 . . . . .	0.21-0.36		

It will be seen that there are only 2 instances (Cases Nos. 887 and 904) with a blood sugar of more than 0.3 per cent. These values were obtained only a short time before death. There were 3 cases with blood sugars which are normal. Case No. 18, in 1897, had an undoubted diabetes, but has been sugar-free for many years. The diabetes was presumably dependent upon gall-stones, and with the disappearance of symptoms of gall-stones the diabetes apparently vanished. A roentgen ray, however, shows calculi at the present time. The second of these cases, Case No. 29, has continued to do a large amount of work requiring unusual mental responsibility, and although he frequently shows sugar, he rarely shows any great amount. This case is further complicated by a genito-urinary condition which requires frequent manipulation, and the trauma from this may account for the occasional appearance of glycosuria. The other case (Case No. 1007), with the normal blood sugar, presented this after she had been virtually sugar-free for a year. At the beginning of the period the blood sugar was 0.23 per cent. She dieted with great care throughout this year, and only rarely did glycosuria appear. At the period during which the blood sugar was 0.1 per cent., she underwent without disturbance a pelvic operation. Recently this patient had an attack of gall-stones, hitherto unsuspected, but the sugar in the urine did not return and the blood sugar rose only to 0.12 per cent. Now, twenty-one days after the attack, she is sugar-free, and upon a diet of 56 gms. carbohydrate, 57 gms. protein, and 84 gms. fat.

The blood lipoids were determined in 9 of the cases. The results constitute a part of the series of cases studied by Dr. W. R. Bloor and Dr. Horace Gray. In the following table the average figures for lipoids expressed in grams per 100 c.c. blood for the cases which have lasted fifteen or more years are contrasted with the average figures for diabetics of varied duration, and also with Bloor's average figures for normals.

TABLE IV.—THE BLOOD LIPOIDS IN CASES OF DIABETES OF FIFTEEN YEARS' DURATION.

	Total fatty acids.			Lecithin.			Cholesterol.		
	Whole blood.	Plasma.	Corpuscles.	Whole blood.	Plasma.	Corpuscles.	Whole blood.	Plasma.	Corpuscles.
Average value for 9 cases of 15 years' duration . . .	0.62	0.63	0.53	0.33	0.26	0.42	0.25	0.28	0.21
Average value for 105 determinations on diabetics of varied duration . . .	0.80	0.95	0.55	0.36	0.32	0.41	0.32	0.38	0.22
Normal average .	0.37	0.39	0.34	0.30	0.21	0.42	0.22	0.23	0.20

From these figures it is observed that the average for these cases is less than for all the diabetics (105 bloods); on the other hand it is higher than the average for the normal bloods. In none of these cases were there sufficient lipoids to be evidenced to the naked eye—in other words, lipemia did not exist. The fact that the averages are less than those of all the diabetics confirms the rule<sup>1</sup> that the greater the duration of the diabetes the less the lipoids are increased above normal. This seems reasonable, for in general a high lipid blood content spells disaster. The following two analyses of the blood of one patient made a year apart show a very definite increase in the amount of total fatty acids and of cholesterol. During this year the patient has been in much better health than at any time formerly, although in order to remain sugar-free she has been obliged to diet very carefully. Her tolerance now, however, is in the neighborhood of 75 gms. carbohydrate, 60 gms. protein and 90 gms. fat, making a total of 1350 calories, or 28 calories per kilogram body weight. Her blood sugar amounts to 0.12 per cent.

TABLE V.—TWO ANALYSES OF BLOOD LIPOIDS OF CASE NO. 1007.

Date.	Total fatty acids.			Lecithin.			Cholesterol.		
	Whole blood.	Plasma.	Corpuscles.	Whole blood.	Plasma.	Corpuscles.	Whole blood.	Plasma.	Corpuscles.
February, 1916 . .	0.40	0.40	0.40	0.30	0.20	0.41	0.20	0.20	0.20
February, 1917 . .	0.45	0.48	0.42	0.27	0.24	0.30	0.22	0.23	0.21

It is encouraging to record the severe illnesses which these 62 cases have survived. Three cases have withstood pneumonia, 8, or 13 per cent., have had gall-stones. Among the 1187 cases the

<sup>1</sup> Bloor, Gray and Joslin: Jour. Am. Med. Assn., 1917, lxi, 375.

incidence of gall-stones was 2 per cent. In some of the cases these were diagnosed prior to the discovery of the diabetes. In others the diagnosis was made subsequently. It should be remembered, however, that gall-stones take years to form, and undoubtedly exist long before they are suspected. One case was operated upon for appendicitis, 2 for fibroids, 2 had ulcers on the leg, gangrene was survived in 4, with 2 amputations, renal complications occurred in 7, and herpes zoster, phlebitis, neuritis, and psoriasis each appeared in at least 1 case. Ten of the patients (4 living and 6 dead) prior to their last illness withstood a considerable acidosis, but in 11 others it was the cause of death. Acidosis, however, was seldom severe. Among those cases in which the twenty-four-hour urine was obtained there was only one patient who had sufficient evidence of acidosis to warrant a determination of the urinary ammonia. In 4 of these cases it was sought and found to be normal. Case No. 310 had a severe acidosis from which she recovered three months before death. Case No. 887, a fatal case, excreted 3.7 gms. of ammonia when first seen. This later rose to 4.7 gms. ammonia while fasting. This case has been reported elsewhere in detail.<sup>2</sup> It is one of the cases in whom we probably caused acidosis by our former method of treatment, and has been one of the important factors in influencing us to avoid strict fasting in cases which have not been accustomed to such treatment. The other two cases with high ammonia excretions recovered from their acidosis.

The carbon dioxide in the alveolar air was determined in 7 cases. In only one of these was the tension as low as 29 mm. Hg. at entrance to the hospital. Two of these cases died while at the hospital; one of these was Case No. 887, above cited, who showed 29 mm. Hg. tension at entrance. The alveolar air remained at 29 mm. Hg. until twenty-four hours before death, when it suddenly dropped to 14 mm. Hg., from which level it never rose. The other patient, Case No. 904, had a severe carbuncle at entrance and no acidosis. His alveolar air varied from 32 to 38 until seven days before death, when, overcome by his infection, he failed rapidly, and two days before death his carbon dioxide tension was 16, and one day before death 14.

The causes of death of the 25 fatal cases were as follows:

Coma . . . . .	11
Arteriosclerosis . . . . .	7
Nephritis . . . . .	3
Cancer . . . . .	1
Cystitis . . . . .	1
Tonsillitis . . . . .	1
Cirrhosis of liver . . . . .	1

The 11 cases dying of coma (44 per cent.) make approximately the same percentage as that found with the ten-year series of cases.

<sup>2</sup> An Analysis of 14 Cases of Diabetes Mellitus Unsuccessfully Treated by Fasting, Boston Med. and Surg. Jour., 1916, clxxiv, 425; also The Treatment of Diabetes Mellitus, 1917, 2d ed., p. 359. Lea & Febiger, Philadelphia.

This contrasts very favorably with the 60 per cent. of deaths due to coma in the 1187 cases, but it shows that if acidosis is prevented these patients could be reasonably expected to live for a longer time. The causes of death of the remaining patients may very well have been independent of the diabetes. Today we feel that the deaths of probably 7 of the patients who died of coma could be postponed.

The diabetes is now a minor issue with the patient in 18 of the 37 living cases. Some of these individuals have, it is true, severe nephritis, but 17 are continuing their regular occupations. The diabetes was also a minor issue at the time of death in 7 of the fatal cases. Four of the living cases have outlived their normal expectation of life for their age at the onset of their diabetes. Of the fatal cases 5 outlived the normal expectation of life; in fact, 15 per cent. of the entire series achieved their fulness of years. Ten of the 62 cases were considered severe at the time of the first visit, and now must be regarded on the border-line of severe and moderately severe diabetes; 27 were moderately severe and 24 were mild. One case, when first seen, was considered moderately severe, but later became mild.

CONCLUSIONS. 1. In a series of 1187 cases of diabetes, of whom 1156 are traced, 640 are living and 516 are dead; among these were 62 who lived fifteen or more years, or 5 per cent., and of these 37 are living and 25 are dead.

2. Obesity is universal in the long-lived diabetic. It was demonstrated in 60 cases out of 62.

3. A diabetic heredity is one and one-half times as frequent among the cases of fifteen or more years' duration as among all the diabetic patients.

4. The average loss of weight when the patient first came to us for treatment was 41 pounds.

5. Gall-stones were recognized in 8 cases, being six times as frequent among these cases as in the entire series of 1187 cases.

6. The presence of acidosis was demonstrated 21 times and 11, or 44 per cent., of the fatal cases succumbed to it. By the avoidance of acidosis the lives of these patients might have been prolonged.

7. Arteriosclerosis occurred in 36 cases, and was a prominent factor in causing the death of 10 patients.

8. Diabetes is now a minor issue in 50 per cent. of the living patients, and at the time of death was a minor issue in 28 per cent. of those who had died. An extremely rigid diet is necessary for only 4 of the patients now living.

9. Of the fatal cases, 20 per cent. outlived the normal expectation of life for their age at the onset of their diabetes, and this is already true for 10 per cent. of the living cases.

10. Dietetic treatment was carried out to a considerable degree by 57 cases. Of the remaining 5 cases, 3 are among the dead,

## INFARCTION OF THE HEART SIMULATING ACUTE SURGICAL ABDOMINAL CONDITIONS.

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IN 1819 Laennec emphasized the occurrence of acute abdominal pain in pneumonia, and Andral, in 1823, and Louis, in 1829, made further descriptions of this occurrence. In more recent times abdominal pain has been found to be associated not only with pneumonia, but also with pericarditis and pleurisy, as has been emphasized particularly by the pediatricians. Edwards<sup>1</sup> and Mackenzie<sup>2</sup> have called attention to the fact that not only could there be abdominal pain, but also tenderness, muscular rigidity, and the other classical signs of acute peritonitis. Various observers refer to the mild epigastric pain, paroxysmal in nature, associated with typical angina pectoris. Very little reference to any other intrathoracic condition than the above has been made as a possible cause of these *acute abdominal symptoms*.

During the first half of the year 1916, 2 cases have been observed in the Peter Bent Brigham Hospital, giving the signs and symptoms of an acute surgical condition in the abdomen. One of these patients died on the operating table within twenty-four hours of admission, and the other, who was not operated on, died within forty-eight hours. Postmortem examination was carried out in both cases and showed very similar conditions. There was marked extensive myocarditis and coronary sclerosis. Both showed infarction of the heart as the result of a thrombus in the anterior coronary artery which almost completely obliterated the lumen and caused numerous areas of necrosis. No other pathological changes were present which could explain the symptoms in either case.

In view of the fact that the numerous text-books and systems of medicine and surgery make no mention of this condition in association with acute abdominal symptoms, and that very few cases are referred to in the literature,<sup>3</sup> the following 2 cases with their pathological findings are reported in detail.

<sup>1</sup> Jour. Am. Med. Assn., 1911, lvi, 1784.

<sup>2</sup> Lancet (London), 1915, i, 796.

<sup>3</sup> Clifford Allbutt refers to a case from the literature of fatal thrombosis of the right coronary artery in which there was pain and collapse, suggesting a perforated gastric ulcer. This patient, however, had had previous attacks of angina pectoris, and the pain in the last attack was located at the lower end of the sternum and left hypochondrium and radiated to the left arm. Diseases of the Arteries Including Angina Pectoris. London, 1915, ii, 450.



CASE I.—Med. No. 4099, Surg. No. 4233. The patient was a hardware clerk, aged thirty-nine years. The family history was negative except that his father died of angina pectoris. He had been married for six years, but had no children. He used tobacco in moderation and no alcohol whatever. In childhood he had had scarlet fever, diphtheria, croup, measles, pertussis, and mumps. There was no history of chorea, rheumatic fever, bronchitis, pleurisy, pneumonia, malaria, typhoid fever, or exposure to tuberculosis. There was a history of gonorrhea but not of syphilis.

There was nothing otherwise noteworthy in his past history until one year ago, when he began to have "indigestion," consisting of cramp-like pains over the apex of the heart, most severe when he was walking, and accompanied by a sensation of "stoppage of breath." He had no difficulty in climbing stairs, but at times when walking had to stop every few feet because of a sensation of tightening over the heart. These symptoms had a sudden onset, and continued for three months. They were not severe enough to keep him from sleeping, but were more distressing by day. During these three months he also had cramp-like pains in the calves of the legs, which came and went suddenly. There was a gradual disappearance of all the above symptoms, but he seemed to be getting slightly weaker. As far as could be made out there were no other evidences of circulatory or gastro-intestinal disease.

Five days before admission to the hospital he felt poorly on arising, and without apparent cause began to have pain across the epigastrium, which radiated toward both nipples. He coughed more or less, raised some mucus and a small amount of blood and phlegm. He was unable to eat much and vomited at intervals. He thinks that he coughed up rather than vomited the blood. Since the onset he was constipated and his bowels moved only by enemata. He felt exhausted and was continually complaining of pain in the upper abdomen.

Physical examination showed a well-developed and nourished man, aged thirty-nine years, leaning on his elbow and doubled up with pain. He was somewhat stuporous and exhausted, answered questions slowly, was uncommunicative, and did not seem to remember details well. Face was pasty and sick-looking. Skin was cyanotic and of smooth texture. The pupils reacted fairly promptly to light, though through a small arc. The right pupil was irregular when contracted. They both reacted well to accommodation. The sclerae were faintly but definitely icteric. The breath was foul and the lips of a dull red color. Gums showed no lead line.

The thorax was symmetrical, and expansion of fair volume and equal on both sides. Respiration was regular, deep, and rapid, being 34 to the minute. No abnormal pulsations were seen over the precordium. The apex beat of the heart was neither seen nor felt. The left border of relative cardiac dulness was  $9\frac{1}{2}$  cm. from

the midsternal line in the fifth intercostal space. The upper border of dulness was at the third rib, and the right border 2 cm. to the right of the midsternum. There was no increased supracardiac dulness. The heart action was regular but weak and no murmurs were heard. Both aortic and pulmonie second sounds at the base were faint. No pericardial friction sounds could be heard. The radial pulses were regular, of small volume and low tension, and the rate was 150 per minute. The systolic blood-pressure was 92 and the diastolic 80, the pulse-pressure being only 12.

Examination of the lungs showed normal resonance throughout. Fremitus was well transmitted. Breath and voice sounds, though slightly diminished, were not otherwise remarkable. In the lower half of the left lung behind a moderate number of medium moist rales were heard. No pleural friction rub was present. The abdomen was on a level with the thorax, symmetrical and without pulsations. In the epigastrium extending to the umbilicus was a prominence about 15 cm. in diameter, somewhat more to the right of the midline. Over this area the percussion note was dull, though elsewhere there was good resonance. There was tenderness and a high degree of spasm in the epigastrium. No definite masses could be felt. There was no evidence of free fluid in the abdominal cavity. Gall-bladder, spleen, and kidneys were not felt. The liver flatness began at the fifth rib and extended to the costal margin, where it fused with the dulness described above. The edge of the liver was not definitely felt. The extremities showed no significant abnormalities.

The patellar and Achilles reflexes were not elicited, even on reënfacement. Cutaneous sensibility was normal. The rectal temperature was 102° F. The blood examination showed a hemoglobin of 114 per cent. (Sahli), a red cell count of 5,632,000, and a leukocytosis of 21,400. The stained blood smear was not remarkable. The urine showed a trace of albumin but no sugar. The blood Wassermann taken at this time was subsequently reported negative.

A few hours after admission, after having been seen in consultation by the surgeons, he was transferred to the surgical service, with the diagnosis of an acute surgical abdominal condition, the possibilities being acute pancreatitis, acute gall-bladder disease, and perforated gastric ulcer. By this time the following changes in his condition were noted: The respirations were at times periodic. Rales were heard at the bases of both lungs, and there was definite dulness over the right lower chest behind. The abdomen was rather distended. In the right upper quadrant a mass was easily palpated, extending about 6 cm. below the costal margin in the right mammary line. Over the upper portion of this mass, which was very tender, there was a soft, almost fluctuant area suggesting the stomach. A slight fall in the pulse rate and temperature,

together with the lung signs, deferred the surgeons from operating that night.

The next morning there was no appreciable change in his condition, and he was sent to the operating room for exploratory laparotomy. Ether anesthesia by the drop method was slowly induced until the beginning of the second stage, and the site for incision was meanwhile infiltrated with novocain. The patient then began to struggle violently, relaxed quickly, and stopped breathing, becoming intensely cyanotic. The ether was stopped and artificial respiration employed. He was now pulseless; the abdomen was quickly opened and the heart was massaged from below the diaphragm. These measures were, however, of no avail. Examination of the abdomen at this time showed no abnormality except an enlarged congested liver.

*Autopsy* was performed six hours after death, the report of which follows.

*Peritoneal Cavity.* On opening the abdominal wall the organs were found to be congested. The liver extended a hand's breadth below the costal margin in the right mammary line. There was no excess of free fluid. The peritoneal surfaces were smooth and normal in appearance. The gall-bladder wall was not thickened; the mucous membrane was smooth; there were no stones, but the bile was viscid and dark. The common duct was patent.

*Thoracic Cavity.* When the sternum was removed about one liter of clear straw-colored fluid was found in each pleural cavity.

*Heart.* The heart was enlarged and weighed 570 grams. The pericardial sac contained about 20 c.c. of clear fluid. The epicardium appeared normal, and beneath it the myocardium, especially that of the left ventricle, appeared distinctly yellowish. Both sides of the heart, the right particularly, were markedly dilated. The tricuspid ring measured 15 cm., pulmonary 7.5 cm., mitral 9.5 cm., aortic 6.5 cm., and the valves were normal. The wall of the left ventricle measured 1.5 cm. in thickness and that of the right 0.5 cm. The apices of both left and right ventricles were filled with thrombi. Thrombosis of the wall of the left ventricle was very extensive, large thrombi being present around the papillary muscles of the left side. The left ventricular side of the septum at the apex was depressed, yellowish, and opaque, with purplish patches. Sections through the myocardium showed an almost complete necrosis from extensive infarction. The muscle in these infarcts was yellowish and opaque, and was surrounded by a thin zone of grayish, semitranslucent tissue. Section through the right ventricle showed white fibrous patches. The coronary arteries were sclerotic, the anterior coronary being irregularly thickened and its lumen almost obliterated. Microscopic sections of the left ventricle showed definite abscess formation in large areas of necrosis. The heart muscle fibers contained numbers of disintegrating and

poorly preserved polymorphonuclear leukocytes. Section through the anterior coronary artery showed an extreme grade of arteriosclerosis, with great narrowing of the lumen and hyalinization and calcification of the wall.

*Lungs.* The lungs were heavy, tough, and exuded a great abundance of fluid from the cut surface, which had a salmon-yellow color. The picture was that of edema and congestion, with some bronchopneumonia.

*Other Viscera.* The mucous membrane of the stomach was injected. No areas of ulceration were seen. The pancreas was entirely normal. There was edema and congestion of the liver, kidneys, and spleen. The aorta showed extensive atheromatous degeneration most marked above the bifurcation. There was one small area of ulceration covered by a thin thrombus. There was generalized peripheral arteriosclerosis shown by microscopic sections.

CASE II.—Med. No. 4784. The patient was a foreman in a riding school, aged fifty-nine years. The family and marital history were unimportant. He smoked four or five cigars a day, but used no alcohol or drugs. He had "pleurisy" many years ago, but he was not confined to bed. He never had rheumatic fever, chorea, tonsillitis, pneumonia, malaria, or typhoid fever. There was a history of gonorrhea but not of syphilis. There was nothing otherwise noteworthy in his past history until one year ago, when he began to have dyspnea on walking up stairs, but this did not prevent his doing light work. He had no chronic cough, hemoptysis, or swelling of the legs. His appetite had always been poor, but he had no indigestion, distress, pain, or eructations. He occasionally vomited as a result of swallowing tobacco juice. His bowels were regular. He had been troubled with hemorrhoids for years, with occasional bloody stools.

Three weeks before the onset of his acute symptoms he had a pain in the right chest which was made worse on taking a deep breath, and which disappeared after lasting several hours. He was in his usual fair health until four hours before admission, when he was suddenly taken with sharp, constant, non-radiating pains in the upper part of the abdomen. This pain was aggravated by a deep breath. He perspired profusely, felt nauseated, and vomited a little soup which he had had for dinner. Later he repeatedly regurgitated small amounts of fluid, but had no hematemesis. He never previously had an attack similar to this one.

Physical examination showed a well-developed and nourished, somewhat drowsy man, aged fifty-nine years, lying flat on his back, with his knees drawn up, continually complaining of pain in the upper part of the abdomen. The pupils were equal, regular, and reacted to light and accommodation. The scleræ were clear. The lips were slightly cyanotic and dry. The tongue had a moderate grayish coat. The gums showed no lead line.

The thorax was symmetrical and expansion was equal on the two sides. The respirations were regular, shallow, and 36 to the minute. The depth of respiration could only be moderately increased by taking a forced inspiration. The apex of the heart could neither be seen nor felt. The left border of relative cardiac dulness was 12.5 cm. from the midsternal line in the fifth interspace. The right border was 2.5 cm. to the right of the midsternum, and the upper border was at the third interspace. No increased submanubrial dulness could be made out. The heart action was regular and the rate was 107 per minute. The sounds were distant; the first sound was specially weak. No murmurs were heard. A suggestion of a protodiastolic gallop rhythm was heard at the apex. At the base the aortic second sound was louder than the pulmonie, but neither was accentuated. No thrills were felt over the precordium. No pericardial friction rub was heard. The pulses were of rather poor quality and low tension, the right radial being more easily palpable than the left. The vessel walls were slightly thickened, but not tortuous. The systolic blood-pressure was 106 and the diastolic 80.

The lungs showed normal resonance throughout. Fremitus was transmitted, with normal intensity everywhere. There were no areas of bronchial breathing, but the respiratory sounds were diminished throughout. Over the right lower back frequent crackling rales were heard, and there was a suggestion of a pleural friction sound.

The abdomen was scaphoid in form and tympanitic on the left side. There were some dulness in the right upper quadrant and slight non-shifting dulness in the right lower quadrant. There was an area of moderate tenderness between the ensiform and umbilicus, extending to the region of the gall-bladder, where a distinct resistance was met. The resistance at the first examination was thought to be the head of the pancreas, dilated gall-bladder, or liver. No definite liver edge could be made out. Liver dulness extended from the fifth rib to the costal border in the right midclavicular line. Spleen and kidneys were not palpated. The extremities, reflexes, and skin sensation were normal. The temperature on admission was 96.8°. The blood showed 100 per cent. hemoglobin (Sahli) and a leukocyte count of 19,600. The stained smear showed 85 per cent. neutrophils and no stippling of the red cells. The admission specimen of urine showed a specific gravity of 1041, a slightest possible trace of albumin, sugar 2.1 per cent., acetone ++, diacetic acid +, and no bile. The sediment showed rare hyaline and finely granular casts, but no red blood cells. The blood Wassermann taken at this time was subsequently reported negative. The stool examination was negative.

The surgeons saw the patient in consultation. An acute perforative or inflammatory intra-abdominal condition was suggested by the sudden onset and severity of the epigastric pain, the tender-

ness and slight spasm, the questionable mass in the region of the gall-bladder, and the white blood count of 19,600, with 85 per cent. neutrophils. The weak pulse and faint heart sounds, the facial expression of prostration, and the subnormal temperature suggested perforated gastric ulcer, acute pancreatitis, or ruptured gall-bladder. The presence of sugar, acetone, and diacetic acid in appreciable amounts in the urine impressed the surgeons sufficiently to defer operation, thinking the condition possibly due to diabetic acidosis.

The next day the diagnosis was considered as lying between some disturbance in the region of the gall-bladder or the head of the pancreas, and acidosis with gastric symptoms. The temperature had risen to 100.4° F. and the leukocyte count was 19,900. The patient grew more drowsy, but answered questions intelligently and complained of abdominal pain and nausea. The indefinite tender mass in the region of the gall-bladder remained as described above. On the following morning the nurse noticed him to be in partial collapse. At times she could not feel the radial pulse, and noticed that he acted queerly, rolling up his eyes for short periods. When it could be counted the pulse was found to be slow. These observations were soon confirmed by the house physician. Now for the first time, thirty-six hours after entrance, the cardiac factor began to be appreciated. The pauses in the heart's action, its slow rate, and the attacks during which the patient rolled his eyes and seemed to swoon, pointed strongly to Adams-Stokes syndrome. Several hours later electrocardiograms were taken and showed complete heart-block. The auricular rate in these tracings was 143 and the ventricular rate 29 and regular.

On this morning the leukocyte count had increased to 33,500. The CO<sub>2</sub> tension of the alveolar air taken during the day was 28.7 mm. of mercury and the blood CO<sub>2</sub> (Van Slyke method) was 28.1 mm. In contrast to this the CO<sub>2</sub> tension of the alveolar air taken on the day of entrance was 37.4 mm. The twenty-four hour urine specimen on this morning showed 1 per cent. sugar, with less acetone than on admission and no diacetic acid. These findings, though indicating some acidosis, were not sufficient to point to diabetic coma as an explanation of the patient's condition. Sodium bicarbonate, however, was given by mouth, but was vomited. Sodium bicarbonate enema was given, but was expelled. While preparations were being made to give sodium bicarbonate intravenously the patient had another attack, with cyanosis, and died in a short time.

*Autopsy* was performed fifteen hours after death, the report of which follows:

*Peritoneal Cavity.* No free fluid or adhesions were found. All viscera were in normal position. The liver extended to one finger's breadth below the costal margin.

*Thoracic Cavity.* No fluid or adhesions. Both lungs were more voluminous than normal, especially the right. The pericardial sac contained the usual amount of fluid.

*Heart.* The heart was decidedly larger than normal and weighed 420 grams. Both ventricles were very much hypertrophied and dilated. The wall of the left ventricle measured 2 cm. in thickness and that of the right ventricle  $\frac{1}{2}$  cm. The mitral valve measured 12 cm., tricuspid 14 cm., aortic  $8\frac{1}{2}$  cm., and the pulmonic 8 cm. The anterior coronary artery was occluded by a thrombus at the upper portion of the intraventricular septum. The muscles supplied by this artery were pale and whitish in color. The line of demarcation between the normal muscle and the area of infarction was well marked, and over the latter area were numerous small necrotic spots. At the apex of the heart in between the papillary muscles there were numerous fresh thrombi, which showed the formation of lamination very well. The posterior coronary artery was free from thrombi. The walls of both arteries were very much sclerosed and contained numerous yellowish opaque slightly elevated atheromatous plaques, some of which reached the size of  $1\frac{1}{2}$  cm. Microscopic sections showed diffuse infiltration by polymorphonuclear leukocytes, with areas of great accumulation of these cells. In these foci there was considerable necrosis of the myocardium, as shown by the karyorrhexis taking place in the nuclei of the fibers. The fibers were highly vacuolated, and in some areas distinctly granular.

*Lungs.* The right weighed 940 grams and the left 540. The right was much more voluminous than normal and its cut surface presented a uniform reddish, angry, moist appearance. Upon pressure some frothy serosanguineous material was exuded from the bronchi. The left lung was softer and presented a congested appearance throughout. There were no pleural adhesions and the condition of the lungs was one of congestion.

*Pancreas.* Grossly the pancreas was essentially normal. Microscopic sections showed a large amount of fat in the organ. There was some increase in the connective tissue. In focal areas the acini had disappeared, the islands being well preserved.

*Other Viscera.* There was acute congestion of the kidneys, liver, and intestines, and acute hyperplasia of the spleen. The aorta was covered with numerous yellowish, opaque, slightly elevated atheromatous plaques specially numerous at the ascending and transverse portion.

*DISCUSSION.* The above 2 cases were strikingly similar in their history, clinical course, physical findings, and necropsy examination. Both patients entered the hospital complaining of acute epigastric pain of a few days' duration in one case and of a few hours' duration in the other. Both had slight nausea and some vomiting, and felt quite sick, but neither had chill nor felt

feverish. Their past histories were essentially negative except for antecedent angina in one. Physical examination showed marked tenderness in the epigastrium in each case and a questionable mass in the region of the gall-bladder, over which the percussion note was dull. The pulses were of poor quality, slightly rapid, and the heart sounds were feeble. In neither case were cardiac murmurs heard, the apex beat was neither seen nor felt, and cardiac dullness was slightly increased in the second case. One case developed complete heart-block shortly before death. The blood-pressure in both cases was low, the pulse-pressure in the first case was only 12 and in the second 26. There were anomalous signs in the right lower chest in both instances, consisting of a moderate number of rales at one time and subsequently a diminution of the breath sounds throughout both lungs. The acute epigastric pain and tenderness, together with a leukocytosis of about 20,000 and a moderate fever in both cases made the diagnosis of an acute inflammatory or perforative lesion of the upper abdomen seem probable. The conditions considered were perforated gastric ulcer, acute pancreatitis, and acute gall-bladder disease. A laparotomy with negative findings was performed on the first case. The mild diabetes with acidosis in the second case, together with the drowsiness, influenced the surgeons to consider that the patient might be on the verge of coma, and dissuaded them from operation.

The pathological examination in both cases showed striking similarity in that the anterior coronary arteries were in each instance practically obliterated by thrombosis, with resultant extensive infarction of the heart. Generalized arteriosclerosis was likewise a common finding. The lungs, liver, spleen, and kidneys showed acute passive congestion. The liver edge in the first case extended to a hand's breadth below the costal margin, which accounted for the abdominal mass palpated. No other lesions were found in the viscera, which could account for the symptoms.

The condition above described bears a close relation to angina abdominalis and angina pectoris. In the former the abdominal pain, according to some, is due to a lesion of intra-abdominal blood-vessels, either a spasm or thrombosis; according to others the pain in the abdomen is a referred pain from an accompanying angina pectoris. In angina pectoris the angular pain, having its classical location in the precordium, with its frequent radiation to the arm, is associated with a coronary sclerosis, and there may be thrombosis in these vessels with resultant infarction of the heart. The cases above presented showed the pathological lesions consistent with angina pectoris, but the pain and other symptoms pointed to an intra-abdominal lesion. Clifford Allbutt<sup>4</sup> points out as distinguish-

<sup>4</sup> Clifford Allbutt: *Diseases of the Arteries, Including Angina Pectoris*, Macmillan & Co., London, 1915, vol. ii, p. 452.



ing characteristics of coronary embolism from the angina pectoris of the ordinary form "the flutter and lability of the heart, the rapid, irregular, and failing pulse, the waning sounds, the dyspnea, and the cyanosis." He as well as Hochhaus<sup>5</sup> and Obrastzow and Streschesko<sup>6</sup> refer to the fact that the pain in infarction of the heart is more continuous than in typical angina. The 4 cases of coronary thromboses reported by Hochhaus all had typical precordial anginal pain with no evidence of an acute inflammatory process. The cases here presented had the further perplexing factors of a leukocytosis and fever. In the second of our 2 cases a definite diagnosis of infarction of the heart was made ante-mortem when the complete heart-block developed. It was only retrospectively that the cardiac factor in the above 2 cases was appreciated, for in the first there was precordial pain on exertion for a year and in the second dyspnea on exertion for the same length of time.

**CONCLUSION.** Two cases are here presented which gave the history and presented the signs of an acute inflammatory or perforative lesion of the upper abdomen, but turned out to have coronary thrombosis with infarction of the heart.

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## A BRIEF EXPERIMENTAL STUDY OF THE MORPHOLOGY OF THE HEART MUSCLE FOLLOWING HYPOTHYROIDISM.<sup>1</sup>

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AND

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SLOW action of the heart is one of the chief characteristic features of hypothyroidism whether occasional or continuous, spontaneous or operative. In some cases other aspects of the heart action give also the appearance of a myocardial disease. Thus exercise, though followed by dyspnea, may not be accompanied by commensurate increase in heart rate. The quality and vigor of the heart muscle tone is often greatly impaired and the valve closures are no longer clear and prompt. The capillary return, particularly in the periphery is delayed, favoring fibrosis and diminishing parenchymatous activity.

The use of digitalis, camphor, caffein, and similar drugs in most of these instances fails to improve these symptoms, but even in

<sup>5</sup> Deutsch. med. Wchnschr., 1911, No. 2, p. 2065.

<sup>6</sup> Ztsch. f. klin. Med., 1910, lxxi, 116.

<sup>1</sup> Read at the meeting of the Association of American Physicians, 1917.

long-standing cases, the giving of thyroid quickly relieves in large part inadequate heart action or now renders the action of the drugs effective.

A diagnosis of myocarditis, or more probably of myocardial degeneration, would be a very natural conclusion in such instances were it not for the other signs of thyroid deficiency and the prompt relief of this among the other signs and symptoms of a defect which follows when thyroid is given.

Inasmuch as these cardiac signs appear quite early in hypothyroidism it is to be expected that whatever the basic cause be, it should become evident in the heart mechanism fairly soon. If the changes induced were of an anatomical nature, relief of any rapid degree in long standing examples would not be expected following thyroid medication. In cases which give histories of thyroid instability, especially such as had at some time shown definite hypothyroidism, permanent signs and symptoms of muscle defect may, however, appear.

It is obvious that this question cannot be satisfactorily answered by the study of material taken from clinical cases of hypothyroidism or myxedema, for the literature in this respect shows great variation in reports as to the pathological anatomy of the heart, and it is obviously impossible to attribute to the thyroid deficiency alone the changes which are frequently reported in a condition which is accompanied by so many complicating problems as this.

From the clinical aspects of the condition there would appear to be but little doubt that the disease is brought about by chemical or physiological rather than by morphological defects, but to clear the ground and to decide certain questions in our own minds, preparatory to a broader study of the subject, we have undertaken the following brief study for the purpose of deciding whether or not the cardiac signs which appear in hypothyroidism are or are not accompanied by recognizable morphological alterations in the heart muscle. In a clinical study of a large group of hypothyroid conditions, now under way, this preliminary point appears to be of considerable importance.

For reasons of convenience, rabbits were selected for the study. The operation of thyroidectomy was very carefully performed under light ether anesthesia. Five deaths took place during or apparently as an immediate effect of the operation; these are not included in the study. All the visible thyroid tissue in the usual location was removed in each case and an attempt was made to avoid the parathyroids. As tetany did not occur in any of the 10 instances reported it seems probable that we were successful in this respect.

In each case the material removed was examined microscopically to identify absolutely the character of the tissue. In all the 10 instances reported this was found to be only an apparently normal thyroid tissue.

After operation the animals were housed and fed as carefully as possible, and were under constant observation and expert care, though no great attempt was made to study them clinically. Immediately after death, if it occurred during the laboratory hours, the heart was removed and placed in a formalin fixative. A general autopsy was made in each instance and the apparent cause of death noted. When the animal died after laboratory hours it was placed at once in the ice-chest by the laboratory orderlies and was autopsied early the next day.

The hearts were examined grossly, fixed in formalin, and sectioned in paraffin. The sections were taken in each instance through the left ventricle vertically, through the tip of both ventricles, and a third plane extended tangentially through the interventricular septum. The sections were stained with hematoxylin and eosin, and were minutely studied under the customary powers of magnification.

EXPERIMENTS. Rabbit No. 2. Female operated June 26. Died August 8. Duration of postoperative life forty-three days, during which time the animal exhibited the customary signs of deficient thyroid secretion. It died with a septic peritonitis and a probable general septicemia.

Microscopic examination showed practically identical lesions in all sections. The most striking alteration consisted in a definite stain attraction on the part of the cell nuclei, with in some fibers a considerable ovoid area of granular degeneration at either pole of the nucleus. In a few instances a small amount of brownish pigment was found in this area. A certain amount of parenchymatous degeneration was demonstrable in nearly all fibers. About some of the capillaries and arterioles a leukocytic infiltration had taken place in some areas associated with some evidences of proliferation of the interstitial connective-tissue cells.

Rabbit No. 3. Male. Operated June 28. Some hemorrhage took place during and after the operation, but the animal lived until July 15, seventeen days, dying apparently from a septic peritonitis.

No consistent lesions were demonstrable in the heart fibers. Occasionally a typical nuclear proliferation was seen and some cells showed moderate albuminous degeneration. The interstitial and perivascular tissues showed a few small areas of cell proliferation and of small round-cell infiltration, clearly an acute change.

Rabbit No. 6. Male. Operated June 29. Slight oozing followed operation, but no vessels were cut. Respiration very rapid, reaching 120 per minute for about three-quarters of an hour. Died July 3, four days after the operation. At autopsy a bronchopneumonia was found, but no peritonitis or apparent wound infection. Coccidiosis of the liver was present.

Microscopic examination showed no change of a chronic nature

in any part of the heart muscle, but in a few areas, notably in the interventricular septum, there was marked congestion of the capillaries and smaller bloodvessels, with some acute parenchymatous degeneration of the muscle cells.

Rabbit No. 7. Male. Operated June 29. Slight oozing. No vessels cut. Respiration shallow and rapid, 194 per minute. Cough was at first present, but the respirations soon fell to 120 and the cough disappeared. Animal died July 2, three days after operation. No gross lesions were apparent at autopsy.

Microscopic examination showed practically no lesions present, nothing which in any way could be considered as a result of the operation or of the thyroid defect.

Rabbit No. 9. Male. Operated July 3. Died July 16, thirteen days after operation. Autopsy showed a hemorrhagic area in the mediastinum. The inferior cava was engorged. Myocardium pale, bronchopneumonia, coccidiosis of liver, with cirrhosis. Suprarenals negative.

Microscopic examination showed no lesions present.

Rabbit No. 10. Operated July 3. Died July 6, three days after operation. Autopsy showed septic pneumonia, from which a pure culture of *Bacillus coli communis* was isolated.

Microscopic examination showed no changes whatever in the heart fibers but many of the capillaries and smaller venules were packed with blood cells in which a pronounced leukocytosis was apparent. Other blood channels were filled by the growth of a bacillus corresponding morphologically to the *Bacillus coli communis*.

Rabbit No. 12. Male. Operated July 14. Died July 16, two days after operation. No lesions seen at autopsy. Wound apparently in good condition.

Microscopic examination shows marked congestion of many of the capillaries and venules of the myocardium, but no changes except an occasional muscle fiber showing parenchymatous degeneration.

Rabbit No. 13. Male, operated July 14. Died July 16, two days after operation. Autopsy showed no apparent lesions. Wound in good condition.

Microscopic examination shows absolutely no changes.

Rabbit No. 14. Male. Operated July 18. Died July 25, seven days after operation. Autopsy showed no obvious lesions present.

Microscopic examination showed no lesions except occasional parenchymatous degeneration.

Rabbit No. 15. Operated July 29. Moderate hemorrhage. Died June 30, one day after operation. Abdominal wall wet, but no demonstrable peritonitis; wound moist. No peritonitis or pneumonia.

Microscopic examination of the heart showed no lesions whatever except for occasional parenchymatous degeneration.

Although the amount of material presented in this study is small and the extent of time during which the animals lived insufficient (from two to but forty-three days), since it apparently corroborates the natural conclusions derived from the clinical study of these cases, we have felt that this line of investigation is no longer profitable.

Our conclusion may be summarized as that the cardiac signs and symptoms produced as a result of hypothyroidism are not due to morphological alterations in the heart muscle, nor does this status produce secondary anatomical variations of any characteristic degree or type in the heart muscle.

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## REPORT OF CERTAIN UNUSUAL CASES OF MALARIA, WITH A BRIEF ANALYSIS OF FIFTY CASES OF THIS DISEASE.<sup>1</sup>

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DIAGNOSTIC difficulties surround the diseases with which we are not by personal experience familiar, and this applies not only to some new syndrome, but recently recognized, but with almost equal force to any condition which possibly, because of geographical location, we have been seldom or never privileged to see. Perhaps this is most true of those diseases which, once common, are now becoming, through improved hygiene, sanitation, and treatment, more and more rare and infrequent. To the younger generation of physicians this must spell unfamiliarity and diagnostic difficulty. It may be said that the more nearly a disease is stamped out the less efficient will the coming physicians be to recognize it and carry on the work of extermination. Yellow fever, smallpox, and malaria are examples which at once come to mind, and it is from this point of view that these cases are presented.

In Philadelphia today, malaria cannot be said to be common, and yet enough cases annually occur to make it very important to be on the lookout for this infection, for it is only from a human carrier that the mosquito becomes infected and a source of transmission.

During the past five years there have been admitted to the medical division of the Hospital of the University of Pennsylvania, under the care of Prof. Alfred Stengel, 58 cases, with a final diagnosis of malaria. In all but 8 of these cases the diagnosis was

<sup>1</sup> Read before the Section on General Medicine of the College of Physicians of Philadelphia, November 27, 1916.

proved by the discovery of the parasites in the peripheral blood, and it is only with these 50 cases that this paper concerns itself.

In reviewing this short series of cases there are certain points which stand out clearly, and there are 5 cases which deserve individual mention. Two of these cases were brought to the hospital in complete unconsciousness, and in one of these an estimation of the blood-urea nitrogen gave the very misleading reading of 42 mgm. per 100 c.c. of blood. Another case gave a pure growth of *Streptococcus viridans* in blood culture, and in still another the diagnosis was confused by a coincident lead-poisoning. The fifth case, one of local origin, was sent in as a case of pernicious anemia with a hemoglobin of 20 per cent., and complaining only of headache and paresthesias. These cases will be detailed in full, but before doing so certain points concerning the whole group deserve mention.

**SOURCE.** Of these 50 cases of proved malaria, 30 were sailors coming to the hospital from the British Consulate, and having acquired the infection in various parts of the world. In 8 cases the history pointed to Tampico, Mexico, as the source and in 6 to Cuba; the others were scattered from Africa to Chile. In passing it may be noted that often there was a history of other cases on the same ship which had been treated by the captain, and had not required hospital care. Of our remaining 20 cases, 9 were University students who came from the following homes: Alabama 2, New York 2, Missouri 1, Louisiana 1, South Carolina 1, Porto Rico 1, and Brazil 1. It would seem probable that all of these infections except the 2 from New York should be considered as having been obtained at home. In the 11 cases remaining the infection could be traced to Palestine in 1 case, Virginia in 2, Delaware in 1, and 7 cases were of strictly local origin in Philadelphia or its suburbs. This number of cases seems large when compared with figures given by the Philadelphia Board of Health, but it must be remembered that physicians and also hospitals are very lax in the reporting of such diseases as malaria to the proper authorities. Also it is true that the University Hospital in receiving all patients from the British Consulate is apt to have a greater number of such cases. The average number of cases of malaria reported annually to the Board of Health of Philadelphia during the past ten years has only been about 40, but the actual number of cases has certainly been very much higher.

**PARASITE.** The type of parasite was diagnosed as of the tertian variety in all but 11 cases, in which sure proof was found that the organism was of the estivo-autumnal variety; 10 of these 11 cases came from out of the country, the other being from either Virginia or from Pennsylvania. These cases were no more severe, showed no more anemia, and responded no less satisfactorily to quinin than did the tertian cases. Of course, the positive finding of the

sexual forms or crescents of estivo-autumnal malaria makes the diagnosis of this form of infection certain, but in the absence of crescents, and when only a few ring forms are seen, the diagnosis of the type of parasite is much less sure, and it must be admitted that some of the severe cases which were considered of the tertian variety may have been estivo-autumnal or mixed forms.

That the plasmodium was not found in 8 cases which were diagnosed malaria is not surprising, and it is pardonable that the diagnosis of malaria was made eight times in spite of this failure to discover parasites, although it is, perhaps, a more serious fault to diagnose malaria without finding the parasites than it is to fail to diagnose correctly a case of malarial infection. In justification let it be said that 7 of the 8 cases were in sailors. All 7 had been freely exposed to the infection and all gave clear histories of characteristic chills and fever, but had no chills while in the hospital. In 5 the spleen was palpable. The eighth was a student from North Carolina with a history of chills and an enlarged spleen, but with no chills while under our observation. Repeated examinations of the blood of these patients failed to reveal organisms, and the diagnosis had to be made without this support. Writers disagree as to the percentage of cases harboring malarial parasites in which it is impossible to discover the plasmodia in the peripheral blood, but all agree that such cases do occur, and especially in chronic and estivo-autumnal malaria. Incidentally it may be remarked that, as a rule, the presence of malarial parasites in the early stages will not be discovered during the making of a routine differential count, and that a poorly trained man when searching for malaria is as likely to make an incorrect positive diagnosis as he is to fail to recognize the parasites when present.

**SYMPTOMS.** Of the series, few presented any unusual symptoms except the cases to be reported in detail. All but 8 gave a history of having had chills or had chills in the hospital. The majority complained of the characteristic symptoms, but many laid special emphasis upon pains in the legs, headache, or loss of appetite, and in some these were the only complaints.

Nine of the cases did not present any demonstrable enlargement of the spleen and these cases did not fall into a group as to duration, severity, or type of parasite. In determining the enlargement of the spleen palpation alone was depended upon, as percussion of the spleen is without doubt very untrustworthy. In several instances failure to palpate the spleen may well have been due to rigidity of the abdomen or obesity. A surprising number of cases showed slight degrees of icterus, most of them, however, without any demonstrable bile pigment in the urine. A further point often noted in the physical examination was a soft systolic murmur over the base of the heart, and this seems to have been independent of the degree of anemia.

**ANEMIA.** Perhaps incorrectly anemia is generally accepted as one of the most frequent symptoms of malarial infections, and it is usually said to be more severe in the estivo-autumnal type than in cases infected with the tertian or quartan varieties. It is also often said that chronic cases are more anemic than acute, but in this connection one point must be kept in mind. It is in the acute cases, with paroxysms, that the greatest blood destruction occurs, but in such cases the bone-marrow compensation is good and the loss is promptly made up, while in the chronic cases there may be a failure of the bone-marrow to compensate for even a slight but persistent destruction of erythrocytes.

The blood findings in this series are very variable; only 8 cases had a hemoglobin below 50 per cent., and 14 had readings of above 80 per cent. In only 4 cases was the reading very low (20, 26, 29, and 30 per cent.), and of these there was but one with a red cell count of less than 2,000,000. The color index was therefore well below one in each of these cases. These 4 very anemic cases did not by any means represent the most severe nor the most prolonged infections; 2 were infected with the estivo-autumnal parasite and 2 with the tertian. On the other hand the cases with a high hemoglobin included some instances of prolonged infection and 2 cases of the estivo-autumnal type. Aside from the changes characteristic of anemia the erythrocytes exhibited nothing peculiar, and nucleated red cells were but seldom seen.

The patients were all questioned about former attacks and 14 gave a history of attacks more than a year previous, and 5 described primary attacks within a year. This latter group should be considered according to Celli's rule to have come under our observation in a relapse rather than to be cases of reinfection. The former group contained some cases of relapse, but also many of apparent reinfection. A study of the degree of anemia in relation to these previous attacks led to no conclusion, but there is no doubt that a negative history is often misleading, and that many cases harbor the parasites unsuspected over long periods. For example, there were 2 patients in the series who claimed to have been in perfect health for a considerable period, but who promptly developed malarial paroxysms after being chilled and wet in the ocean, one by falling overboard and the other in a shipwreck. It has long been recognized that exposure, change of climate, and various diseases tend to relight an old and quiescent malaria.

**LEUKOCYTES.** The highest count of white blood cells in this series of 50 cases was 12,200 per c.mm., and only six counts of 10,000 or over were recorded. On the other hand 4000 was the lowest count, and there were only six counts below 5000. The accepted teaching is that there occurs in malaria a slight diminution in the total leukocyte count and an actual increase of large mononuclear cells. In this series the mononuclear cells ran on the average a



little high, and in 1 case 35 per cent. of these cells was present and in 2 cases 18 per cent. It is said that the increase in these cells is most marked in the intervals without fever, but counts were not made frequently enough in this series to confirm this observation. Nor was the presence of granules of malarial pigment within the cytoplasm of the large mononuclear cells, as has been described, observed in our cases; 1 or 2 per cent. of eosinophiles was quite constantly noted.

In several patients in whom the history and clinical appearance did not strongly suggest malaria the finding of a mononucleosis encouraged further search for parasites with ultimate success. As has been said no instance of marked leukocytosis was observed, and no case in which the polymorphonuclear leukocytes were increased. In fact a polymorphonuclear leukocytosis almost never occurs in uncomplicated malaria, and if present in a doubtful case, time will be better spent examining the patient for some other source of trouble than in doggedly searching the blood for plasmodia, simply because the fever chart is suggestive.

FEVER. A text-book fever chart is usually only obtained at the expense of the patient by withholding quinin, and in this series the charts are not very instructive. A surprising number of cases with parasites in the peripheral blood failed to show any febrile reaction, and a small number had distinct rises in temperature without any chills or any symptoms of fever except slight headache and malaise. In every case the temperature promptly became normal once vigorous treatment with quinin was instituted, and the patients were all discharged without fever, without organisms in the peripheral blood, and apparently in good condition. Only 1 case returned in a relapse, but as the majority of the cases were in sailors, many of whom left port soon after discharge, it is impossible to draw conclusions as to the permanent efficacy of the treatment.

DIAGNOSIS. The diagnosis in the majority of the cases was made easy by a typical history and by chills and fever occurring soon after admission. The cases which gave the greatest diagnostic difficulties are reported below with brief comments.

CASE I.—*Chronic estivo-autumnal malaria of cerebrospinal form with convulsions and coma.*

E. P., a sailor, fifty-seven years, was brought to the hospital in coma, having been suddenly seized with a convulsion some hours previous. No further history was obtainable at the time. Temperature was 103° F. Patient was breathing stertorously and large moist rales were audible all over the chest. The pulse was weak and of low tension, and the heart sounds could scarcely be heard. The blood-pressure was 95 systolic and 55 diastolic. Spleen was not palpable, but the abdomen was distended and palpation difficult. There was a great deal of hiccough. Unconsciousness was

complete and no voluntary motions were made. The urine was obtained by catheter and contained a light cloud of albumin and many casts. The blood count was: hemoglobin 63 per cent., erythrocytes 2,910,000, and leukocytes 11,200.

By the next morning the temperature was normal, the circulation greatly improved, and consciousness restored, although the patient was still a little irrational. A history was then obtained of a typical attack of malaria, with chills and fever, two months previously in Cuba. Examination of a stained spread of his blood revealed many parasites of the estivo-autumnal variety in both the sexual and the asexual forms. Despite active medication with quinin the patient had several slight rises of temperature, but he had no return of the cerebrospinal symptoms or of the circulatory collapse. He ultimately left the hospital in a very good condition.

CASE II.—*Tertian malaria of cerebrospinal form with repeated attacks of coma and circulatory collapse.*

E. C., female, aged sixty-nine years, was admitted to the hospital in a state of semi-unconsciousness, having been taken suddenly ill on a train. On admission she was mentally confused and her circulation was in a very alarming state of weakness, pulse very rapid and thready, and myocardial tone very poor. The temperature was 99.6°. The urine showed a faint trace of albumin and many casts. The blood count was: hemoglobin 80 per cent., red blood cells 4,890,000, and white blood cells 11,800; differential polymorphonuclears 82 per cent., lymphocytes 8 per cent., large mononuclears 8 per cent., and transitionals 2 per cent.

A diagnosis of myocardial weakness and cerebral anemia was made and the patient given cardiac stimulants. Within two hours her condition improved materially, and the next day she had recovered sufficiently to desire to continue her journey. She then gave a history of having been in Brooklyn on a visit in apparent good health until the twenty-first of the month, when she was taken with a chill and felt drowsy. A physician was called and diagnosed liver trouble. She continued drowsy, and on the twenty-third became worse, vomited, and had some epigastric pain. On the twenty-fourth she felt well, but on the twenty-fifth had a second chill but felt well enough to start for her home in Delaware. On the trip she became partially unconscious and was sent to the hospital. She states that she had three or four attacks during the past year, somewhat similar to the present one, but these former attacks were always associated with slight outbreaks of erysipelas on her ankles, to which she attributed the chills and malaise.

This history was obtained on the twenty-sixth, and at this time the patient seemed in excellent condition. The morning of the twenty-seventh the patient was found to be irrational and at times stuporous. Her temperature abruptly rose to over 103°, and she showed signs of circulatory collapse. The blood-pressure fell and

did not respond to any stimulation until after the temperature fell. There was no chill and the spleen was not palpable. The patient became clear mentally, but could not remember what had happened. The following day, the twenty-eighth, she appeared entirely recovered. On the twenty-ninth the chill was repeated, and for the first time a few tertian parasites were found in the blood. No further attacks developed after treatment with quinin was instituted.

These 2 cases are both examples of the so-called cerebrospinal form of malaria. Many names and subdivisions have been applied to cases presenting such evidences of cerebral or spinal irritation as delirium, coma, and convulsions, but they are better all grouped together under the term of cerebrospinal. These cases are also often spoken of as one type of pernicious malaria, in that they acutely endanger life, and certainly in the 2 cases reported the patients' condition on admission was most threatening. The great circulatory weakness is said to be almost constantly present in such attacks, and it is very characteristic that the return to nearly normal conditions is amazingly abrupt. Within but a few hours the second patient would change from a condition of satisfactory circulation and blood-pressure into what appeared to be an alarming circulatory collapse, only to recover almost as rapidly.

In Case II an interesting observation was made on the urea content of the blood. It has been shown in the past that there occurs an increased urinary output of urea during a paroxysm, and that this increase begins several hours before the attack, attains its maximum during the cold stage, and declines to normal at the end of the paroxysm. Our case was being investigated from a renal stand-point and blood was taken for the determination of the blood-urea nitrogen at a time when the temperature was normal. An hour later the patient had a chill, and the high reading of 42 mgm. per 100 c.c. of blood is probably to be correlated with the increased output of urea which is known to occur at this time. A later estimation after all chills had been stopped by quinin showed that the reading had fallen to 25 mgm. This second reading is still far above normal, and this observation deserves further investigation.

CASE III.—*Estivo-autumnal malaria, with coincident streptococcus viridans septicemia.*

E. N. E., aged fifty-one years, a railroad conductor traveling weekly between Virginia and Philadelphia, was exposed fifteen days before admission to the wet and slept in his damp clothes. He awoke chilly and stiff in all his joints, and three days later felt sick enough to take to his bed. At that time he had no pain, no chills, and, in fact, no symptoms except a slight headache. Except for typhoid fever at nineteen years his previous medical history was negative. On physical examination nothing abnormal was noted other than a moderate enlargement of the spleen. The urine

examination was unimportant and the blood count was: hemoglobin 54 per cent., red blood cells 3,840,000, and white blood cells 7700; differential count: polymorphonuclears 66 per cent., small lymphocytes 23 per cent., mononuclears 7 per cent., transitionals 2 per cent., eosinophiles 1 per cent., and basophiles 1 per cent. At the time he was running a continuous irregular temperature and a tentative diagnosis of typhoid fever was made. The agglutination tests with *B. typhosus* as well as for *B. paratyphosus* alpha and beta were negative, and the blood culture gave a pure growth of *Streptococcus viridans*. The diagnosis was accordingly changed to streptococcus septicemia and a fruitless search for a focus of infection was commenced. Studies by Dr. Herbert Fox of the patient's serum in relation to the organism obtained by blood culture showed the marked presence of anaphylatoxin and slight agglutination in all dilutions, but the examinations made for opsonins, complement deviation, and bactericidal properties were either negative or unsatisfactory. These findings strengthened our belief in the correctness of the diagnosis of septicemia even though a second blood culture was negative. An autogenous vaccine was prepared and the patient given injections, with moderate reactions, but with no improvement. Finally, after two months of intermittent irregular temperature, the patient had a frank chill, and crescents of estivo-autumnal malaria were for the first time found in his blood, although the blood had been previously examined several times, with negative results. Under quinin treatment the temperature remained normal and the patient rapidly improved.

CASE IV.—*Tertian malaria and lead-poisoning.*

H. B., a sailor, aged twenty years, was admitted with the history that two months previously he had been infected with malaria in Tampico, Mexico, and that he had chills and fever occasionally since. His chief complaint was severe pain in the epigastrium. Examination revealed a typical lead line on the gums and a palpable spleen. The blood examination showed tertian malaria and also marked basic degeneration of the erythrocytes. On questioning the patient stated that he had been engaged for some time in painting the ship, and that his epigastric pain developed four days after he had commenced painting. He had had pains in the abdomen in the previous malarial paroxysm, but this present pain was different.

The only point of interest in the case was the degree of basic granulation in the red blood cells. This may occur in malaria or to a less extent in any anemia, but never to the extent to which it appears in plumbism. Furthermore, there are differences in the granules between those due to lead and those due to other conditions. This differentiation, however, is not always so easily made in a given specimen. Of course, basic granulation must be clearly distinguished from the so-called stippling which occurs in the

infected cells in both tertian and estivo-autumnal malaria. In this patient the lead line on the gums and the history, as well as the character and frequency of the basic granulation, led to the conclusion that malaria and lead-poisoning were coincidentally present.

CASE V.—*Estivo-autumnal malaria without chills, simulating pernicious anemia.*

F. R., a colored girl, aged eighteen years, living in the suburbs of Philadelphia, was sent into the hospital with a diagnosis of pernicious anemia. She stated that she had been in perfect health until one week previous, but this statement is without doubt unreliable. She stated that on that date she developed an intense headache and numbness of the fingers and toes. She had never been sick except for typhoid fever when very young. Physical examination revealed all the evidences of intense anemia—a palpable spleen and markedly diminished knee-jerks, but no demonstrable sensory changes. The blood count showed a severe anemia of secondary type: hemoglobin 20 per cent., red blood cells 3,510,000, and white blood cells 9500; differential count: polymorphonuclears 78 per cent., lymphocytes 12 per cent., mononuclears 8 per cent., and eosinophiles 2 per cent. Polychromatophilia, anisocytosis, poikilocytosis, and a small number of nucleated erythrocytes were observed. The day following admission the temperature rose to 104.4°, and at this time a very few tertian organisms were found in the blood. No chill was experienced. A similar febrile reaction without chill occurred forty-eight hours later. Under quinin and hematinic medication the fever ceased and there was rapid improvement of the anemia with a corresponding disappearance of the headache and paresthesia.

This case is detailed because in this locality an anemia of this severity is very seldom found to be due to malaria, and, in the absence of chills, the true diagnosis might well have been overlooked. This significance of enlargement of the spleen as suggesting malaria in a case of severe anemia is undoubted. In many non-malarial anemias the spleen may be palpable and even quite large, as, for example, in hemolytic ictero-anemia. But in pernicious anemia or in simple secondary anemia the spleen never approaches the size of a malaria spleen, nor is it ever as firm and hard. Similarly the splenic enlargement of such acute infections as typhoid fever rarely is as great as that commonly seen in malaria. On the other hand it must be remembered that the spleen is not always enlarged in malaria.

Perhaps the diagnostic difficulties presented in these cases are not such as to confuse experienced physicians in a malarial district, but it can be stated without apology that where malaria is uncommon, such unexpected cases do give difficulty in diagnosis.

## PRIMARY CARCINOMA OF THE LIVER IN INFANCY AND CHILDHOOD.\*

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THE occurrence of carcinomatous neoplasms in infancy and childhood is uncommon as compared with adult life. Carcinoma of the liver appears to be more frequent than sarcoma; yet certainly rare in any form, and still more so if the primary cases alone are considered. In view of these facts the following instance seems of sufficient interest to warrant putting upon record. The child was referred to me by Dr. Thomas J. Butler, of Bethlehem, Pa. The clinical history follows:

May 13, 1914. Mary G., aged twenty-one months. Family history negative. The child had previously had good health, except for some degree of anemia, supposed to be dependent upon indigestion, and a constant tendency to constipation. In the winter just passed her appetite for weeks had been abnormally great, although she would take little other than milk, and for some time she had had attacks of vomiting nearly every morning. This condition had, however, improved at the time when, five weeks before, her father accidentally discovered a lump which could be felt beneath the costal margin on the right side in front. It is stated that this had not increased in size, but that there was an unusual amount of veining of the walls of the thorax and of the distended abdomen, and that the child had lost weight and had not seemed well. Her appetite had continued good, and there had been no history of pain.

*Examination.* The infant is well nourished, with a slightly pale skin. Just below the costal border, midway between the midsternal and the right mammillary lines, is a decidedly visible prominence, which on palpation is found to be a hard, smooth mass, apparently with a rather firm edge. It appears to be connected with the liver. Bimanual palpation in the renal region produces no movement of it. It changes its position distinctly with respiration. The liver, as a whole, is decidedly enlarged, and its edge can be felt as far as the left mammillary line at the costal border.

*Provisional Diagnosis.* Either a tumor or a cyst of the liver.

May 18. The child was referred to Prof. Edward Martin, of the University of Pennsylvania, for examination and for operation if possible. A roentgen-ray picture seemed to show opaque bodies in the tumor mass, suggesting the diagnosis of a teratoma connected with the kidney or with the suprarenal body. Incision was made by Dr. Martin today. The right lobe of the liver came well

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into view, and situated in its substance was a dark-gray, glistening, fibrous capsule, covering a mass the size of a large orange, which projected slightly above the surface of the organ, and extended in depth through the entire thickness of the lobe, becoming visible upon the under surface when the liver was lifted. There was no evidence of infiltration of the hepatic tissue beyond the capsule of the growth or of involvement of any organs as far as could be seen. No adhesions were present. Incision through the capsule showed a soft, whitish substance, much resembling in color and appearance the tissue of the thymus gland or pancreas. A small portion was excised for histological study.

Inasmuch as the case appeared to be an inoperable one the wound was closed. The later operative history was uneventful, except for slight delay in healing. The child returned home on June 5, looking rather paler than on admission, and with the region of the tumor more prominent.

The histological examination was made by Dr. John Speese. The small size of the portion removed prevented an exact study of its relations. His report reads: "Nodule consists entirely of epithelial cells without trace of liver tissue. The arrangement of the cells is for the most part without order, but in a few places there are attempts toward reproduction of the acini, indicating that the process originated in glandular epithelium." Prof. Allen J. Smith, of the department of pathology, later examined the specimen and agreed as to its nature, saying: "The growth histologically is a carcinoma simplex, but at one or two points are attempts at tube arrangement of such a character that I may venture the belief that the growth was originally a cancer of the bile ducts."

*Later History.* This has been furnished me by Dr. Butler. The mass continued to grow in a downward and forward direction and later toward the left hypochondrium, the abdomen becoming finally distended by it. At times the increase of size would appear to be rapid, and then would follow periods of quiescence. As time passed the superficial veins grew more prominent, until finally the larger were about the size of a lead-pencil. The tissue about the navel became discolored and very thin. No ascites or edema was present. There was sleeplessness and increasing debility, but apparently little if any pain. Death occurred February 4, 1915. No autopsy was permitted.

Primary carcinoma of the liver in early life, rare as it is, has been the subject of considerable study, including several tabulations of reported cases, notably those of Steffen, Philipp and Castle. Steffen analyzed and tabulated 39 cases of malignant growths of the liver in children. Of these 12 were described as sarcoma and 27 as carcinoma. A further study of his analysis shows, however, that 1 case was included twice, and that another, that of Acland and Dudgeon, was classified as sarcoma, although apparently

undoubtedly carcinoma. There are also included by him a case published by Bohn, which may have been secondary to carcinoma of the pancreas, and one very briefly recorded by Leichtenstern as carcinoma of the peritoneum and liver. Certain other cases in Steffen's list he regards as of a secondary nature, and in still others there was no autopsy or microscopic examination. With these exclusions, but including provisionally the cases of Bohn and of Leichtenstern, there remain 24 which may be denominated primary carcinoma of the liver. It must be admitted, however, that some of them date back for many years, even as far as 1841 (Olivier), and the true nature of these is therefore uncertain. The cases from his list which I have included here are those of Wiederhofer, 2 cases; Hofmann, Kottmann, Pepper, Henschen, Bohn, Lewis, Affleck, Pyc-Smith, West, Wulff, Birch-Hirschfeld, Roberts, Noeggerath, Leichtenstern, Schlesinger, Engelhardt, Deschamp, Acland and Dudgeon, Olivier, Grawitz, Sotow, and a case reported from the St. Joseph's Kinderspital.

Castle excludes some of Steffen's cases and adds others to the list; 1 case, however, was included twice (Burt). Cases in Castle's list but not in Steffen's are those of Burt, Mattiolo, Plaut, Lubarsch and Philipp, Gee, Bonome, Gross, Kestner, Milne, Karsner 2 cases, Peiper, Lapage, Yamagiwa, Idzumi, Nagasawa and Nakamura, Miwa and Utsumi, Miwa and Saito, Fussell and Kelly, and Castle. This makes a total of 44 cases, which seem with more or less reason properly included under primary carcinoma. Kestner's case is entirely without details and can be placed here only provisionally; and that of Miwa and Utsumi I have seen reported only in few words in the abstract of the publication of Nagasawa and Nakamura.

Abstracts of these 44 case reports need not be repeated here. They will be found more or less complete in the publications of Steffen or of Castle. I take this opportunity of adding 12 cases from medical literature which certainly or very probably belong in this category, and that of my own.

Nos. 45 to 49. The following 5 cases are reported by Marckwald, who entitles them multiple adenomata; but in view of the size of the growths and the amount of change present in the liver, as well as of the well-known close association of adenoma and adenocarcinoma, and the difficulty of distinguishing them, it seemed justifiable provisionally to include them in the list of cases given.

No. 45. Girl, aged twelve years; history unknown. Was emaciated and showed edema and ascites. At autopsy numerous nodules the size of a small bean to that of a cherry were found in the liver, entirely replacing the hepatic tissue. The tubular arrangement of the cells of the tumors was very distinct.

No. 46. Girl, aged nine years, exhibited debility, ascites, and edema. Death from marasmus. Autopsy showed very numerous tumors, mostly the size of a pea to that of a walnut, largely replacing



the tissue of the liver. The histological structure was as in the last.

No. 47. Girl, aged ten to twelve years, suffering from ascites and a marantic state. Autopsy revealed numerous tumors larger than a pea, replacing the hepatic cells. Structure that of an adenoma.

No. 48. Girl, aged eleven years, suffered for four weeks from increasing size of the abdomen, edema, and ascites. Death from uremia. The liver exhibited very numerous small and larger nodules throughout the whole of the organ. The structure of the tumors was that of an adenoma, as in the other cases.

No. 49. Boy, aged fifteen years, who had had diarrhea, icterus, enlargement of the liver, and ascites. Death in collapse. The liver exhibited very numerous smaller and larger, sharply circumscribed nodules, from the size of a cherry-stone to that of a cherry. In histological structure they resembled the other cases.

No. 50. Philipp. Male infant, aged nine months; well nourished; very pale, with decidedly enlarged liver. The child wasted rapidly and a tumor the size of a small apple could be felt, apparently connected with the liver. Death occurred after two months. Autopsy revealed a tumor in the right lobe extending through its entire thickness, encapsulated, and having the appearance macroscopically of a cavernous angioma; no metastasis. Histological examination showed it to be a "primary, epithelial, destructive, and, therefore, carcinomatous mixed tumor," containing some traces of cartilage. Philipp believed it to be of embryonic derivation.

No. 51. Wegelin. Boy, aged five and a half years; ill two months. A tumor was found in the upper part of the abdomen on the right side, with dilatation of the abdominal veins; pain; anemia and slight icterus. Autopsy showed numerous nodules in the liver 4 to 6 cm. in diameter, with metastases in the lungs. Histologically the growth was an adenocarcinoma. This case was referred to by Karsner, but has not been included in the published tables.

No. 52. Petrone. Girl, aged four months. Tumor occupied the right lobe of the liver. There were metastases in the lungs. The growth is described as an adenocarcinoma.

No. 53. Hippel. Girl, aged one and three-quarter years; ill for a month, and with the abdomen gradually increasing in size. Examination showed enormous abdominal distention, with greatly dilated veins and the presence of a hard tumor extending across the whole of the abdomen. Cachexia gradually increased and death followed. At autopsy there was found a large tumor of the liver arising from the left lobe; no evidence of metastasis. Histological examination showed this to be a mixed tumor, chiefly of the structure of an adenoma, but containing evidences of cartilaginous tissue, squamous epithelium, and epithelial pearls. Yamagiwa thinks the case very similar to that reported by him, and believes it should be considered an adenocarcinoma.

No. 54. Mair. Boy, aged six years; with abdominal pain; ascites; enlargement of the liver; emaciation and dilatation of the abdominal veins. Autopsy showed the liver substance largely replaced by irregular tumor masses; metastases in the lungs. The case is described as a primary carcinoma.

No. 55. Langmead. Girl, aged five weeks. Autopsy revealed eight pearly white tumors in the liver, the largest the size of a marble. He believed the growth to be an adenoma, and considered (p. 45) it very similar to the case reported by Lapage.

No. 56. Freeman. Boy, aged three years; with abdominal swelling; a mass in the right hypochondrium; little pain; dyspnea. The autopsy showed no secondary growths. The case is described as a primary carcinoma, and a fuller account of it is promised.

No. 57. Griffith.

A case is also recorded by Tate as one of primary carcinoma of the liver in a girl, aged ten years. Exploratory operation showed nodules in the liver, but no microscopic examination was made and no autopsy followed. The diagnosis, although probably correct, is necessarily uncertain. Another is published by Muir, occurring in a girl, aged nine years. It appeared to be a simple adenoma, and he states that there was no reason to suspect the presence of carcinoma. Neither of these cases is included in the list.

As the subject of primary carcinoma in early life has been so well discussed by others, but small space will be given here to its further consideration. In the matter of etiology, reference may be made to the fact that 25 of the cases were in males and 26 in females. In the other instances the sex is not stated. The age of the patients recorded here varies from birth to that of sixteen years. In 2 instances the age is not stated. Of the remaining 55, 4 were new-born. Including these there were 8 in the first three months, and 16 in all in the first year. The remaining are divided as follows: One to two years, 8; three years, 2; four years, 2; five years, 2; six years, 2; seven years, 2; eight years, 1; nine years, 3; ten years, 1; eleven years, 4; twelve years, 5; thirteen years, 1; fourteen years, 3; fifteen years, 2; sixteen years, 1. The occurrence of so many early cases suggests the existence of a tumor of an embryonal nature. This has, in fact, been claimed for a number of them. Others are simple carcinoma; others clearly adenocarcinoma; and still others, some of which I have ventured to include provisionally, have been described as adenoma. Doubtless some of these latter were without question carcinomatous, but in the case of others it must remain undetermined. The tumors may appear in various forms and may be divided, according to Eggel, into nodular, massive, and diffuse. The first is the most common; the last rare. Metastases are not uncommon, especially to the lungs and to other parts of the liver. It is practically impossible to describe the symptoms,

as these are entirely uncharacteristic and depend to some extent upon the mechanical effect of the growths. There is found emaciation and cachexia natural to carcinomatous neoplasms. Icterus and ascites have been noted in some instances, but more frequently they were absent, or no statement made regarding them. Operative interference was attempted in only one instance, and that without success. It could be done only in cases of a single encapsulated tumor. In my own patient the tumor appeared to be too large to permit of any attempt of this sort being made. With the seriousness of the condition in view, however, it would seem justifiable to make such an effort at removal whenever in any way possible.

Inasmuch as there were found a number of errors in the published statements regarding the age and sex, two instances of duplication, and several mistakes in the references to literature, I have verified the statements of those reporting cases by consulting the original publications in nearly every instance. The reference by Steffen to the case of Sotow I was unable to verify, and the original papers containing the report of the Japanese cases, as well as those of Bonome and Olivier, were not accessible.

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## ENTEROPTOSIS AND SUBNUTRITION: THEIR RELATIONSHIP AND TREATMENT.<sup>1</sup>

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WE will consider two conditions, enteroptosis and subnutrition, for the two are closely related.

*First Patient.* First, however, we will relieve this patient of the tube through which he has been fed for fifteen days on account of his state of extreme subnutrition. When admitted he had lost sixty pounds in six months, and, as you see, all his bones are distinctly visible and he has very little flesh left. He had a dilated stomach and ulceration, which was the cause of his malnutrition, and he has been fed by this tube in order to give the esophagus and stomach the proper rest to admit of healing. He will now have special feeding by the mouth and plenty of nourishment in order to restore him to a normal state.

Enteroptosis is a condition in which most of the organs of the abdomen have slipped down more or less and are out of their normal

<sup>1</sup> Lecture delivered before the American Medical Association at the Post-Graduate Clinic, June 4, 1917.

positions. The stomach, instead of extending to the navel, may extend to the symphysis; the kidney, more often the right than the left, but sometimes both, slips down; and often the liver also descends. When the stomach slips down the colon, which is attached to the greater curvature, also descends. It is then a condition in which many organs are concerned, not one alone. It was first described by Glénard. He was not the first to note it, but he was the first to attach a great deal of importance to it, and to point out that it is a common occurrence. He found that many persons who suffered from dyspepsia had this condition of prolapse of the intestinal organs—visceroptosis or enteroptosis—and he attributed the occurrence of the dyspepsia and neurotic symptoms to this abnormal position of the organs.

The fact is, however, that while enteroptosis is often found associated with dyspeptic and neurotic symptoms it often occurs without them. Persons may feel and look perfectly well and still have this abnormal condition.

The condition is found more frequently in women than in men. About 25 per cent. of the women with digestive disturbances show enteroptosis—some say 33 per cent., which I am inclined to think is about the correct proportion. In men we find a proportion of 5 or 6 per cent., so that the condition is about five times more common with women than with men.

The question of how enteroptosis originates has not yet been definitely settled. Some think that it is congenital; others that it develops later in life. It seems probable that both points play a part, for while it may occasionally be congenital we find that it often does develop later in life and is not a congenital state. It is often found in conditions of subnutrition. That means that if a great loss in weight and flesh takes place, no matter for what reason, the patient often develops enteroptosis. It may be either a general loss or a loss of something in the abdominal cavity. For instance a woman is pregnant and has a child. The abdomen was big while she was carrying the child, and after the birth of the child it is much smaller. The woman has lost something from the abdomen, and there is more space within the abdominal cavity for the stomach and intestine to occupy than during the pregnancy, and sometimes the organs prolapse in consequence. This is especially liable to happen if the woman does not take proper care of herself and does not remain in bed long enough to give the muscles and abdomen time to become readjusted. Sometimes a big abdominal tumor has been removed—weighing five, ten, or fifteen pounds. Again, there is more space than before, and if the patient gets up too early there may be a prolapse of the organs. Such things do occur, but they do not play so great a part in the production of the condition as does undernourishment.

Supposing a man weighing, say 180 pounds, has an attack of

typhoid fever or some other acute disease, stays in bed five or six weeks, and during that time takes very little nourishment and loses forty to fifty pounds, and gets up weak and emaciated. In such a condition we are also apt to find a relaxation of all the muscles, and a slipping down of the organs, so that undernourishment evidently plays a very definite part in the development of enteroptosis.

On the other hand, may persons with enteroptosis have accompanying dyspeptic symptoms and are very neurotic. They eat very little and subnutrition develops. That is why it seems wise to consider the two conditions together.

*Second Patient.* When we look at this woman's abdomen we see below the ensiform process a little concavity, and farther down little convexity—a little bulging out—and this is the stomach which you can see here. I will demonstrate that that is the stomach by tapping, which here produces a slashing sound. Do you hear it? I can produce it here, way down in the lower part of the abdomen, but not here under the left costal margin. That is what we call gastropptosis—a slipping down of the stomach. Now we will see about the kidney. (Makes the patient breathe deeply, first palpating and then trying to arrest the kidney.) There is a slipping down of the liver but not of the kidneys. The stomach with its colon and the liver are prolapsed. Very often in these cases we find also a slipping down of the heart—cardiaptosis—especially when the liver is involved. There is cardiaptosis here too. The condition here is not very marked. I simply wish to show you how to find it. The apex of the heart is lower down. That, however, is of no great consequence, and if the patient is properly built up and nourished the heart is the first organ to go back to normal position. If the patient puts on ten or fifteen pounds it will be all right.

*Third Patient.* Now we will examine this other patient. She has a movable right kidney and the stomach is prolapsed.

We will first consider the symptoms of enteroptosis, then touch lightly upon the question of subnutrition, and then the treatment of the two conditions.

As already stated, enteroptosis may exist without giving any symptoms; and again it may be accompanied by a great many phenomena, either dyspeptic or neurotic; but the fact that it may be found without any symptoms indicates that this alone is not responsible for all the symptoms that are ascribed to it. A person with the stomach way down and with a prolapsed kidney may eat well, sleep well, and feel well and strong—so that it is evident that these conditions are not responsible for all the symptoms with which they are credited. How can that be explained?

It is a fact that many patients with enteroptosis show many dyspeptic symptoms—belching, headaches, constipation, or constipation alternating with diarrhea, weakness, sleeplessness—while

others do not. The probability is that while enteroptosis as such does not give rise to disease, yet it is a condition in which when disease exists it cannot disappear so quickly; a patient with such a condition does not recover as rapidly as do normal persons. That is why if persons with enteroptosis suffer with some minor trouble of the digestive tract it is liable to remain; and that is why we find so many among them with these troubles. They do not recover readily.

But there are some symptoms which may be ascribed to enteroptosis as such, for they are so commonly found accompanying it, and are quickly removed by adjusting the position of the organs without any other treatment. These symptoms are very few: (1) Getting tired easily, especially in the back; (2) a feeling as if there were something dragging down in the abdomen—not all persons have this, but some do; (3) some complain of frequent urination, especially when they are up and about; (4) another symptom is that they feel poorly when they get up—they are all right while in bed, but feel badly when they are up during the day—if they lie down they are all right. That is more or less characteristic of enteroptosis. There are a few other points. One of these which I described quite some time ago is that many of these patients (5) find a difficulty in breathing; they complain that they cannot take a deep breath; there may be nothing wrong with the heart or lungs, and yet they complain that they cannot take a long breath. This is found especially with young people of twenty or twenty-five, where one would not expect such difficulty with the breathing apparatus. That is especially apt to be found when there is a prolapse of the liver—hepatoptosis. If that is remembered it will be easy to recognize that condition; otherwise it might be difficult.

A great many of the dyspeptic symptoms should be treated as such, and in addition to that the enteroptosis itself should have proper attention.

Now we will consider the symptoms of subnutrition. Subnutrition is a state of affairs which exists when the organism does not receive enough nourishment to subsist upon. The amount of nourishment required is mathematically known, and if the individual does not get that much there is a loss in weight. If anyone does not get the required amount of nourishment the body has to supply it from its own flesh. Say that a pound of nourishment is required and only half a pound is taken; the body has to make up the difference from its own stored material and there is a loss in weight; and if that disproportion between the required amount and the amount taken is kept up for a long time the loss will continue until the proper nutrition is supplied or the individual will ultimately die.

Subnutrition exists in cases of organic diseases when proper nutrition is made impossible—say a patient with a cancer of the stomach who cannot eat and take enough food—the stomach will

not stand it. If you give that patient a little very fine food; part of it is assimilated to support the body, but the nutrition is deficient; and if that continues it leads to other symptoms in addition, and finally to death—the subnutrition develops further and further. Other organic diseases have the same effect. The disease as such makes it impossible for the patient to take an adequate amount of food.

These conditions, however, form the minor group of patients; in the great majority of patients suffering from subnutrition there is no organic disease, but the faulty nutrition has been acquired. For some reason or another the patient thinks he cannot eat and keeps to an insufficient amount of food until the body gradually goes down and down. If you have such a patient and there is no organic disease the patient can be cured provided his mode of living is changed.

We will now consider a few of the points which lead to subnutrition in functional conditions when there is no organic disease present. These can be cured. First there is the condition which is called sitophobia—fear of food. The patient may have an acute indigestion, and everything he eats hurts him. Such a patient is put on a diet of liquid food, and very little of that, and he recuperates; then he eats as before and has another attack. Someone tells him he has eaten more than he should and he returns to his liquid food, and keeps that up for a month or two, and then continues with it. Now while a man who is well-built can stand a loss of ten pounds or so without any ill effects, if for a prolonged period he continues to take less food than is required he is bound to suffer more or less harm. He begins to think he cannot take anything else than his limited diet, and is afraid that if he eats anything else something will happen; and if he eats a little more and has some discomfort he will eat still less and will have less nourishment and less weight, and he goes steadily downward, and ultimately he may be very sick—not from any organic disease but simply because all the organs of the body are undernourished and in a debilitated state.

Such persons cannot feel well, and they eat and sleep poorly; their nerves are played out and their muscles are weak in consequence of their continued undernutrition. These patients are apt to suffer from a great many symptoms—they feel tired all the time, cannot concentrate their minds, etc.—they lead the existence of an invalid, grow weaker and weaker, and may even die without any organic disease. This may seem exaggerated, but it is not. Some time ago I saw a lady patient in consultation at one of our hospitals. She had a slight temperature, but she had a fear of food and nothing would agree with her; but no organic disease could be discovered. I therefore assumed that no disease was present, and advised that her nutrition be increased. She picked up under



that treatment for a while, but later lapsed into her old state and ultimately died. An autopsy was performed but nothing was found, and the explanation was that it was a mere case of starvation, due to subnutrition. It was quite natural that that should occur. Why not? Complete starvation leads to death quickly and partial starvation leads to a slow death.

While enteroptosis as such may exist for years without much harm to the system or danger to life, subnutrition as such is quite different. If that state of affairs continues without being checked it must lead to death, no matter what be the trouble. So long as any individual continues to take less nourishment than his body requires he is bound to suffer for it. It is very important to realize this, and one cannot lay too much stress upon it in learning to recognize and treat these cases.

**TREATMENT.** The treatment of enteroptosis consists in restoring the adjustment of the abdominal organs. The patients are made to wear bandages to support the abdomen and lift it. It is not material what kind of bandage is worn; a plain towel will frequently serve if it is correctly adjusted, so as to fit snugly and support the abdomen; the long corsets that are now worn are frequently all that is needed. If, however, the long corset does not support the abdomen sufficiently a pad may be slipped under to help. It is immaterial how it is done so long as there is some support to push the displaced organ upward.

The second point is to give these patients ample nourishment, especially those that have lost in weight, as most of them have, although there are a few exceptions. The way to do that is to feed them up well—give them ample nourishment. Very often a gain of fifteen to twenty pounds will restore the organs to normal positions. That has been demonstrated often. Ten or twelve years ago I had a patient with cardioptosis and hepaptosis. I gave him a proper bandage and made him eat freely, and after he had gained fifteen pounds in weight his heart was back in its proper place, and when last seen he was in good shape and looking well, and everything was normal; he had gained thirty to forty pounds and looked the picture of health. Enteroptosis frequently originates from a loss of flesh, and a return to normal is secured by adding flesh.

This is another proof that enteroptosis is not always congenital, for if it were it would be difficult to bring about a change. In an acquired condition it is different, and it seems probable that three-fourths of these cases are acquired.

If some dyspeptic condition is present in addition to the enteroptosis, remedies should be given to adjust the digestive apparatus—and these should be treated as in other patients—but the main treatment consists in building up. That is more important than anything else, not excepting the bandage.

Operative intervention is not called for in these cases. In former years the kidneys used to be attached very often, and even in recent years there are a few men left who attach the kidneys, and some even claim that the stomach, colon, and liver should be lifted and attached. Recently I heard a man in San Francisco claim that all these organs should be attached and readjusted. In my opinion such persons would be worse off after these operations than before. We are so built that we have a certain amount of elasticity in ourselves, but if we begin to attach organs the body cannot manage, and many troubles are originated afterward that did not exist before. It is not a thing which should be done as such. Some persons, however, may have an enteroptosis with an organic lesion, such as an obstructed pylorus, and they may have to be operated upon—but enteroptosis as such should not be operated upon.

As already stated the correction of the subnutrition will also help the enteroptosis. You may have a patient who says he cannot eat anything—everything he eats hurts him. He cannot eat eggs because they give him a headache; he cannot eat meat, for he has so much uric acid; he cannot eat bread, for he has too much fermentation. I have had such patients—some of them physicians—who came to me after they had lost forty or fifty pounds in weight and could not eat. Examination showed no organic disease. How will you treat a patient who says he cannot eat such things? Will you tell him to continue his light diet of milk and toast, etc.? If you do, you will never cure your patient. He has been doing that, has lost weight all the time, and is still losing. You cannot be governed by the patient's sensations no matter how clever he may be—no matter if he is a great doctor. These sensations develop in patients who eat too little; the stomach forgets how to act; it becomes lazy and does not want to have food; it becomes too sensitive. If you give in to that stomach it will continue to be lazy and there will be no relief—no cure for the patient. But if you realize that that is not the right thing to do and that you must change that false condition and make the patient eat, no matter how he feels, you can cure the patient; the eating must be done and the food must be increased at any cost.

Suppose you tell such a patient to eat, and he says he cannot do it; he tells you he has pain and he vomits. What will you do then? At first you will have to give him some remedies to allay the sensitiveness of the stomach; give him a nerve sedative. Anything is permissible provided you make him eat, for that is the foundation of his future health; if you make him eat you will accomplish something; if not, nothing will be done. Accordingly any remedy that will lead to an increase of nutrition is permissible. It may be that the remedies cannot be given for a long period of time; it does not matter; give them for a while, and as soon as you can discontinue them do so. So you may give such a patient codein or morphin, or anything, provided you can overcome the diffi-

culty in taking the necessary food. You do not always need morphin or codein; often a plain nerve sedative, a bromide or tincture of valerian, may be all that is required. The patient must brace up his courage; tell him that it is better to eat and suffer than not to eat and to feel comfortable; and in a short while he will find that it is not so bad after all, and in a week or two he will have no pains or headache and will be like other people.

In changing the diet, however, you cannot do it too abruptly. The man who has been living on milk and toast cannot start in and eat everything else at once. You must change the diet gradually, step by step. First tell the patient to take a little more food such as he has been accustomed to; instead of taking five ounces of milk he should take ten ounces; then let him take raw eggs beaten up in milk, crackers and butter, a little oatmeal, etc. Add something else every day and increase the variety of food, and in a few weeks the patient will have overcome the condition of sitophobia that must be combated before anything can be satisfactorily accomplished. You must first convince the patient that he can eat and that he must eat, and then you will make him gain. I usually have these patients eat five or six times a day; let them eat three meals a day like other people—a couple of eggs in the morning, with a little oatmeal and bread and butter, and a cup of coffee (but I tell them to take it two-thirds of milk and one-third of coffee); then at luncheon, say a piece of chicken or a lamb chop, and mashed potato or other vegetable, etc.; and for supper, fish or eggs, bread and butter, and rice with milk, etc. Besides this, between meals, I have them take milk and bread and butter, or milk and eggs, and bread and butter. I tell them to take plenty of butter—to take a quarter of a pound of butter daily and eat it at their various meals. So if they take enough to sustain themselves in the three meals, and supplement that with these additional meals, a gain in weight is soon accomplished. In nine cases out of ten when I wanted to make the patient gain in weight I have succeeded. There are exceptions when we cannot do it, but they are rare—something is interfering; but if it is systematically done we can nearly always succeed.

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## SOME POINTS RESPECTING THE LOCALIZATION OF SYPHILIS UPON THE AORTA.

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EVER since Vesalius first described internal aneurysm, referring particularly to aneurysms of the thorax, numerous observations

have been made upon the manner of origin and the seat of aneurysm upon the aorta. For many years statistics have been collected indicating the frequency with which aneurysms are found upon different arteries, in a hope that the anatomical distribution of these lesions would give some clue for their occurrence. Although Pare observed that internal aneurysm was not uncommonly associated with the pox, irrefutable evidence of the importance of this disease for the development of aneurysm was not established until 1875 when Francis Welch, in his study of syphilis occurring in the army, described a specific type of reaction in the aorta resulting from lues. For a time following the observations of Welch little support was given to his statement, but during the last few decades the truth of his findings has been confirmed by many authors by different methods of analysis. The earlier studies dealt with the naked eye appearance of the aorta which, when it was involved in syphilitic disease, showed characters quite distinctive and different from those seen in arteriosclerosis. Then, too, the microscope assisted in defining a type of lesion peculiar to syphilis and distinguishable from other diseases of the arteries. True gummata were also occasionally found, leaving no doubt as to the nature of the process acting upon the arterial wall and eventually bringing about such weakening as to permit of aneurysm. The final demonstration of the spirochete in a variety of arterial affections removed all questions concerning the localization of the virus of syphilis in the tissues of the aorta and other vessels.

At first sight it would appear that the problem of syphilis and the arteries has been completely unfolded in the progressive steps illustrated in the many studies since the days of Pare. Most of the work has been developed in logical sequence from the early and rather gross observations to the minutiae of histology and bacteriology. We recognize fully the clinical importance of syphilis as a systemic disease and have many means for the diagnosis of its presence and for the discovery of its relatively early localization upon the arteries. We are, furthermore, aware that the localization of syphilis upon the vessels occurs with greater frequency in certain arteries, the aorta and cerebral vessels, than in others, as well as that the infection occurs in certain regions of these arteries with greater frequency than elsewhere. The predilection of the syphilitic virus for localizing in distinct districts in the aorta has always received much comment. It is true not only that aneurysm of syphilitic origin locates most commonly on the first part of the aorta, but also that syphilitic aortitis in the earliest stages of its development is seen with equal frequency on this portion of the vessel. The mechanical theory of aneurysm which placed greater stress for the production of aneurysm upon the effect of high blood-pressure or, as others would have it, upon the effect of the velocity of currents, than upon the disease in the wall of the artery, had for a

time enticed our attention into channels of thought and theory no longer tenable with the newer studies. Granted, of course, that two factors must be available for the development of aneurysm, first the weakening of the vessel wall and second the presence of a blood pressure (normal, subnormal or excessive), we must not lose sight of the fact that for the development of true aneurysm, the presence of a localized weakening of the artery is of first importance. It is only a weakened vessel which can develop aneurysm; hence, appreciating that the spirochete of syphilis is the most common damaging agent of the aortic wall, the important point occupying our attention is, Why should it localize with such great frequency in isolated segments of the aorta. There is nothing in the character of the tissue of the aorta which could lead us to believe that the chemical characters of particular portions offer a better nidus for the infection, nor is there anything in respect to the microorganism whereby preference would be shown in localizing in one or other portion of the vessel.

The common localization of syphilitic arteritis upon the ascending aorta with the transverse and descending thoracic aorta following next in frequency is now well known. The aortitis beginning in the first portion of the aorta usually localizes at a point just above the aortic ring and then spreads with considerable rapidity along the arch of the aorta for variable distances. The lesion also makes its way in the opposite direction, so that the tissues at the aortic orifice, particularly the valve leaflets, become more or less involved. The spread toward the heart, however, progresses more slowly and we have several examples where, although there was clinical evidence of incompetency of the aortic valve, this was due not to disease upon the aortic valves but to a stretching of the aortic ring. In these instances the syphilitic disease of the aorta stopped fairly abruptly at the upper margin of the sinuses of Valsalva and did not produce any lesion in the aortic tissues contained within the heart. An interesting feature of the syphilitic process of the aorta is the sharp line of demarcation which separates the diseased area from the healthy. This boundary marks the advancing border of the syphilitic process extending to occupy new tissue. The involved aortic wall, with its marked thickening, corrugation, and scarring, is also in sharp contrast to the aorta in other portions. This contrast is decided whether the non-syphilitic areas show sclerosis of other kinds or not. The syphilitic process does not come to occupy any particular face in the circumference of the aorta, and thus does not show a characteristic distribution like the nodular endarteritis which is so commonly observed in the vicinity of the mouths of the intercostals and at the entrance of the ductus arteriosus. The syphilitic process almost always surrounds the lumen, though, as we have pointed out before, the intensity of the involvement at particular points differs in the individual cases.

Another peculiar feature of syphilis of the aorta is the infrequency with which two foci develop concurrently upon separate portions of the aorta. Occasionally a dual localization is found to have occurred, one in the thoracic portion and the other in the abdominal. Less frequently two separate foci occur within the thorax itself; and for the moment I do not recollect ever having seen such a condition recorded. At first sight it might suggest itself that, because aneurysm is sometimes encountered with multiple sacs, one, it may be, situated upon the ascending aorta, a second upon the transverse, and a third upon the descending thoracic, we are dealing in such an instance with separate localizations of the syphilitic virus. Careful examination of these specimens demonstrates that the syphilitic process is diffusely disseminated over the entire thoracic aorta and that the aneurysms have individually developed at situations where local damage has advanced more than in the remaining portions of the arterial wall. That individual and isolated infection may occur in different portions of the aorta is not to be denied, but when this takes place within the thorax the lesions in their early stages progress with such rapidity that they fuse at their borders and can no longer be distinguished as separate occurrences. The occasional double localization upon the aorta is seen where a specific infection has involved the first portion of the thoracic aorta while a second attack has occurred in the abdominal aorta, usually in the vicinity of the celiac axis. Under such circumstances a portion of aorta free from luetic change intervenes between the two foci. It is possible that a relationship between the two lesions may exist, but up to the present it has not been demonstrated. Broadly speaking, however, the syphilitic attack upon the arterial wall differs very materially in its distribution from that of ordinary arteriosclerosis and endarteritis. The syphilitic lesion may occur simply as a patch of greater or less extent, the progress of which is dependent upon the lateral spread from that patch as well as upon the intensity with which the arterial wall is affected by the disease. On the other hand the more common arteriosclerotic affections are not so constant as to the particular portion of the aorta in which they locate, and for them it is the rule to appear at multiple sites with lesions which are quite distinct and unrelated.

Our attention has been attracted, both from postmortem studies and experiment, to the part played by the lymphatics in disseminating syphilitic and other infections along the course of various arteries. We have found that the lymphatic channels of the outer wall of the aorta form a fairly intricate system which communicates with neighboring lymph glands. This system of channels may be demonstrated by injection experiments whereby the interlacing communications stand out quite prominently. From these injection experiments it would appear that the most profuse system of channels is found in those positions of the aortic wall which lie in

closest relation to the neighboring lymph glands, while as a greater distance is interposed between the lymph gland and the area provided a smaller number of lymphatic vessels is to be demonstrated. This is particularly evident in the descending thoracic aorta where a portion of the aortic wall is free and unattached, whereas its posterior and lateral portion lying close to the vertebral column is in close proximity to the lymph glands of this region.

If we follow the aorta from its beginning we find that its first portion lying within the pericardial sac appears to have lymphatic channels in common with the pericardium as it is reflected over it. Macroscopic lymph glands have not been demonstrated between the pericardium and the aortic wall. Directly over the pericardial sac where it is reflected from the aorta to become the parietal pericardium, and lying along the left lateral border of the ascending aorta are a group of lymph glands which communicate with other glands in the anterior mediastinum and which, furthermore, supply this first portion of the aorta. In this region the anterior and left border of the aorta appears to have a richer supply of lymphatic vessels than the right border. About the arch of the aorta there are a number of lymphatic groups, each of which has abundant communications with the aortic wall. The ascending arch has lymphatic connections particularly with glands in the anterior mediastinum, while the transverse arch has a drainage both to the mediastinal glands and to those about the right border of the trachea. The descending arch receives lymphatics from the glands along the left border of the trachea as well as from the glands at its bifurcation. As we pass to the descending thoracic aorta we find a variable number of lymph nodes lying along the border of the aorta and particularly on the right side. The lymph channels from these nodes form a plexus about the exit of the intercostal arteries and advance in single lines around the anterior and free portion of the aortic wall. In the abdominal aorta an intricate plexus of lymph channels is found in the region of the celiac axis which supplies fairly uniformly the aorta in its entire circumference. In the lower portion the aorta receives a rich supply of lymphatics from the retroperitoneal lymph glands which lie along each border of the aorta. These lymphatic channels of the aortic wall lie for the most part in the adventitia, in close relation to and following the course of the fine nutrient vessels which are found in this structure. As the denser portion of the aortic wall is approached the lymphatic vessels become fewer in number and extend only as very fine structures into the adventitia as it adjoins the media. The one feature that is striking is that the lymphatic supply of the aortic wall is not uniformly disposed. In certain portions a much richer supply of lymphvessels can be demonstrated. These ramify in an arborescent or stellate manner, leaving other portions of the aortic wall with a more meager distribution.

To determine the part played by the lymphatics in conveying infection about the arterial walls, bacteria were inoculated into the loose tissue of the mediastinum of rabbits. The organisms used were varieties of streptococci, chiefly of the viridans group. In these experiments it was found that the microorganisms after setting up a localized reaction at the point of inoculation migrated in various directions, most rapidly along the flow of the lymph to the neighboring glands. Gradually, however, the dissemination was of a retrograde character, whereby the microorganisms followed the lymphatics into the various tissues in the vicinity. Thus, the infection was found to follow the fine channels passing about the aorta as well as the structures at the hilus of the lungs. In the rabbit, however, the lymphatics are not nearly so numerous about the aorta as they are in man. The small sized aorta in these animals is poorly supplied by vasa vasorum which penetrate to the media, but the adventitial vessels are well marked. Yet, the results of the experiments were sufficiently clear to indicate a distribution of the infection by way of the lymphatics to the large vascular trunks of the thorax.

A similar but clearer evidence of the lymphatic distribution of infection was obtained in man. It was found that in the severe cases of pneumonia coming to autopsy an almost constant infection of the glands of the anterior mediastinum was to be noted. Under these conditions the lymphatics stand out prominently, the glands are swollen and succulent, and great chains of them can be traced along the trachea and its bifurcation, as well as below the arch of the aorta. The tissues are usually loose and edematous, and if the autopsy has been held shortly after death the subject is a favorable one for demonstrating by the injection method the course of the lymphatics. But more than this, the infecting agent, the pneumococcus, may be isolated from the tissues along the course of the lymphatics and even up to and in the tissues of the outer portion of the aortic wall. Such infections in the aortic wall have previously been demonstrated by Andrewes, and are in accord with our own previous studies in which inflammatory reactions have been observed to follow the course of the nutrient vessels in typhoid fever, acute rheumatic fever, pneumonia and sepsis. In other words, those inflammatory reactions which we have described as types of acute non-suppurative mesarteritis are the result of infection by various bacteria localizing upon the aortic wall by way of the lymphatics.

Further examples, illustrating the progress of a bacterial virus along the periarterial lymphatics, are readily at hand. The importance of these perivascular channels is also illustrated in the spread of the infection in periarteritis nodosa where it may be shown that the involvement of an artery results from the passage of the infection along the lymphatics to the ramifications of that particular artery. We were able to observe this in two cases in which the hepatic artery with its branches was the seat of an acute progressive inflammatory



lesion. In a like manner one can readily follow the perivascular migration of infection in the arteries of the meninges. Here it will be found that the infecting agent and the inflammatory exudate progress along the course of the meningeal arteries as they lie embedded in tissue and that this reaction in the lymph spaces precedes the appearance of the exudate in the larger spaces or caverns of the meningeal folds. Likewise, and of better illustration, is the similar reaction which follows the course of the nutrient vessels passing from the meninges into the brain substance. Similarly the importance of the lymphatic channels, particularly of those surrounding the nutrient vessels of tissues, may be cited in reference to the myocardium and kidney. These are of course common observations, but for the most part we have not been recognizing their importance from the view-point of the further dissemination of the virus nor from the stand-point that when the infectious agent is in such close proximity to arteries of various sizes, actual infection of the arterial wall is liable to occur.

If we again revert to our problem respecting the localization of infection in the aortic wall we must emphasize these three anatomical conditions: (1) as we have pointed out, that there are certain regions along the course of the aorta in which the arrangement of the lymphatic channels is more complex and their number far greater than in other portions; (2) that the aortic wall itself is richly supplied with nutrient vessels, the vasa vasorum, each of which has a liberal lymphatic drainage following its course; and (3) that these lymphatics are in direct association with the larger lymphatic system which surrounds the aorta as a whole and which has two large drainage beds, one in the thorax and one in the abdomen. It is in relation to these drainage beds that the syphilitic virus comes to be distributed to particular segments of the aorta.

The route followed by an infection and the advance of the reaction from one tissue to another can be followed much more readily when the invasion is due to bacteria causing acute responses than when the reactions are more chronic and come under observation only in the later stages of the lesions. This is particularly true in the case of syphilis, in which we rarely recognize the earliest metastatic lesions. Syphilis of the aorta has rarely been observed at a time before the typical changes of the inner or intimal surface are quite distinct. Under these conditions we must appreciate that the syphilitic process of the vessel wall is quite late and advanced, while many of the reactions involving different structures in the infection have been obliterated by the secondary fibrosis. Nevertheless, with some care the track of the reactions may still be followed both within the vessel wall and in the surrounding tissue. In a few cases we attempted to follow the relation of the inflammatory process as it made its way along the vasa vasorum from the periarterial structures to the vessel wall proper. Under these conditions it was

not difficult to demonstrate a chronic mediastinitis which, though of very irregular distribution, nevertheless had a distinct course along lymphatic channels to and from the mediastinal lymph glands. These inflammatory processes appeared mild in degree and would not have attracted attention save that in following the channels more closely it was found that periodic exacerbations occurred along their track. A varying amount of fibrosis was the outcome of the reaction. Where the more aggravated responses led to local cellular infiltration occasional true gummata appeared. It was, however, quite unusual to find marked gummatous destruction of the mediastinal tissues; in fact, we have observed this in only one instance. The lymph glands themselves may respond in the earlier stages of the disease by hyperplasia, but we have found it unusual for these glands to enlarge to such a degree that they would clinically or even pathologically attract attention. During the subsequent process of the syphilitic infection the diffuse fibrosis that is observed in the mediastinum also occupies in some degree the lymph nodes.

By thus localizing in the mediastinum the syphilitic virus has an opportunity of attacking to greater or less degree the important visceral contents of this division of the thorax. The most accessible and important structure is the aorta. The heart itself is peculiarly isolated so that, although it has an extensive lymphatic drainage, it has no dominant compensatory lymphatics advancing upon it from the parietal pericardium. The only region in which accessory lymphatics become available is at the base where the parietal pericardium is reflected directly upon the great vessels. The trachea and large bronchi, which lie in close relation to the lymphatic system of the mediastinum, show a considerable immunity to the localization of the syphilitic virus. The ascending limb and arch of the aorta, on the other hand, are themselves surrounded by a network of lymphatic and bloodvessels and present a vulnerable tissue for the spirochete. Thus with the localization of the syphilitic virus in the rich lymphatic bed of the thorax, it becomes almost certain that the infection will also involve the tissues of the aorta.

The close relation between the luetic inflammatory processes of the mediastinum and those of the aortic wall is also shown in the late fibrosis which leads to such unusual thickening of the arterial coat and which, furthermore, binds the aorta firmly in its mediastinal bed. The thickening of the aortic wall, when involved in syphilis is the result of a connective tissue overgrowth in part situated in the intima and media but for the most part lying in the adventitia and binding this structure to the neighboring periarterial tissues. Syphilitic aortitis has always an associated syphilitic periarteritis. As previously stated, we do not often have the opportunity of tracing the early inflammatory responses which communicate between the mediastinum and the aortic wall, but there is always the evidence in the late cases of reparative fibrosis

which distorts the vascular structures. Of course in the presence of aneurysm, one must be guarded in distinguishing the fibrosis which has resulted from the syphilitic virus from that which has resulted secondarily to the presence of aneurysm from mechanical irritation.

Though we feel confident of the important part played by the lymphatic system of the thorax in localizing syphilis to distinct portions of the arterial wall, it is not clear as yet why and in what manner the virus finds its way to this particular region of the body. By analogy and in comparison with certain other infections, it is probable that the systemic distribution of the spirochete is accomplished by the blood stream. As with other infections, certain tissues and structures are more receptive for the metastatic infection than others. In some instances the localization of the infection may be associated with trauma, but this can hardly be a factor within the chest. Up to the present time animal experimentation has given no clue suggesting the reason for the thoracic metastasis in man. It is probable that the selection of the mediastinum by this infection is bound up with the question of the biological properties of the microorganism and the favorable conditions presented by particular tissues for its growth.

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### CARDIAC DYPNEA.<sup>1</sup>

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EACH of the milestones reached in the continually advancing progress of clinical medicine corresponds closely to some forward step taken in what have come to be known as the "fundamental sciences." A new technical method or a new point of view which opens a fresh way of approach in anatomy, physiology, chemistry, or biology is quickly seized upon by the physician in the hope that it may prove to be an addition to his armamentarium which will aid him to gain new knowledge of disease—its mechanism, its recognition, and its cure. The era inaugurated by Virchow gave to us as accurate a conception of the pathological morphology of the commoner diseases as the methods thus far developed would allow, and the last decade in clinical medicine has belonged essentially to biology and physiology. The study of dead form has largely given way to the study of living processes, the growth of microorganisms and the abnormalities of function produced in cells and organs under

<sup>1</sup> Lecture delivered before the Harvey Society of New York, March 17, 1917.

various conditions of disease. The significant role played by physiology is manifest in many fields of clinical medicine, and the application of the methods and instruments of the physiological laboratory to the study of patients in the wards has broadened and in some instances revolutionized our conception of human pathology.

In scarcely any field has this affiliation between physiology and clinical medicine produced more interesting and stimulating results than in the study of the respiration. The application of modern methods permits the accurate determination of oxygen consumption, carbon dioxide production, the respiratory quotient, and heat production. With their aid we are rapidly gaining insight into the more fundamental changes of the intermediary metabolism which are met with in disease. The adaptation of recent physiological researches on the chemical control of the respiratory center has led directly to the use of methods for determining the carbon dioxide content of the alveolar air in the study of disease. From this and from analogous methods we have learned much about those pathological conditions in which acidosis is a significant feature. Neither in the study of the gaseous exchange nor of the alveolar air, however, is the interest focussed primarily on the respiration itself. Just as the urine is of value in the investigation of nitrogenous metabolism because of the end-products which it contains, so the expired air and the alveolar air are chiefly of interest because they serve as indices of the intermediary metabolism. The respiration itself, the various forms which may occur in disease, the factors which may influence it and limit its efficiency—these have occupied comparatively little attention. It is to some of these changes, and more especially to a consideration of the causes of the dyspnea which occurs in association with heart disease, that the present paper is directed.

Before proceeding to a discussion of those factors which enter into the production of dyspnea, it will be well to state briefly the exact significance of the term itself. As ordinarily used the word is applied loosely to various abnormal types of respiration. Thus not infrequently rapid breathing or tachypnea is referred to as dyspnea, while even more often the increase of rate and depth of respiration which constitutes hyperpnea is characterized as dyspnea. Neither condition is, however, necessarily synonymous with dyspnea. Dyspnea, as the derivation of the word indicates, is a difficult or labored breathing, and there is implied in it an element of subjective discomfort. Hyperpnea, on the other hand, merely signifies an increase above the normal value for the subject at rest in the volume of air breathed. Such an increase of the pulmonary ventilation, or, as it is commonly called, of the minute-volume of air breathed, may be due to a more rapid respiration or to a deepening of the respiration, but usually both factors take part in it. Whether or not in any given instance the hyperpnea will amount to a true

dyspnea depends on the degree to which the pulmonary ventilation is increased, and on the ability of the subject to raise his minute-volume to that degree easily. As will be seen, anything which prevents a person from increasing his pulmonary ventilation in a normal manner will be an element in increasing his tendency to dyspnea.

It is extremely difficult to analyze with accuracy the fundamental cause of the subjective sensation which we know as dyspnea. How much is it due to fatigue of the muscles of respiration? How much is it due to a functional insufficiency of the respiration resulting in an inadequate oxygen supply to the tissues and an incomplete removal of the waste products of metabolism? Without doubt both factors are involved, and one is confronted by a vicious circle, in which waste products accumulated in the cells and blood augment the stimulus to the respiratory center, and this in turn makes still greater demands on the already tired muscles of respiration.

In a general consideration of the respiration it is customary to subdivide the subject into two broad phases—the external respiration and the internal respiration. The former depends largely on the lungs, and the essential feature of it is that the pulmonary ventilation shall be such as to supply oxygen to the blood in the amounts required by the metabolism of the body and to provide for the proper removal of the waste carbon dioxide. The internal respiration in which the circulation plays a prominent role is concerned with the exchange of gases between the blood and the cells of the body. It is clear that if either the external or the internal respiration is inadequate to the task imposed upon it, dyspnea may result. Even when the external respiration produces a blood which is wholly normal as it leaves the lungs, there may be an improper gaseous exchange between the blood and the tissues owing to an imperfect internal respiration. Of the internal respiration, which is possibly the more fundamental phase of the respiration, physiologists and chemists know but little, and of its pathology clinicians know, if anything, somewhat less. The methods for studying even so gross a feature as the rate of the blood-flow are still imperfect, and chemical analyses are limited to blood from the peripheral vessels. The whole field of the internal respiration must therefore, for the present, be left open, and we shall be restricted to a discussion of the conditions affecting the external pulmonary respiration.

One of the chief factors which have aroused interest in the study of the respiration in disease has been the recent advance made in our knowledge concerning the normal control and regulation of the respiration. The old discussion among physiologists as to the nature of the stimulus to the respiration was in a large degree settled by the classical paper of Haldane and Priestley,<sup>2</sup> which showed that

<sup>2</sup> Jour. Physiol., 1905, xxvii, 225.

carbon dioxide is the essential stimulus, and indicated the extreme sensitiveness of the respiratory center in that a rise of 0.2 per cent. of the carbon dioxide content of the alveolar air caused the ventilation to be doubled. Subsequent investigations have tended to broaden this conception, and to Winterstein<sup>3</sup> and Hasselbaleh<sup>4</sup> is due the chief credit of demonstrating that the respiratory center responds not to carbon dioxide alone but to any increase of the acid radicles in the blood.

Since the presence of carbon dioxide and of other acids in the blood depends in general on the chemical processes in the body, it is evident that the basic factor in the regulation of the respiration is the metabolism. The respiratory center controls the movements of the lungs and regulates them so that the pulmonary ventilation keeps pace with the metabolism. In a normal individual at rest a minute-volume of approximately 5 liters of air suffices to remove the excess of carbon dioxide, and to supply sufficient oxygen for the needs of the body. If, however, the subject walks about the room his metabolism rises, more carbon dioxide is formed, the respiratory center is more highly stimulated, and the pulmonary ventilation is increased. The rise in metabolism associated with the walking may require an increase of the minute-volume of air breathed to three or four times its resting value in order that the needs of the tissues for a proper gaseous exchange may be met. Such an increase in minute-volume is easily brought about by increasing the rate and depth of breathing, and, indeed, a normal person is hardly conscious of any change in his respiration when he is breathing 15 liters a minute. With severe exercise the metabolism rises much higher, and in addition to the carbon dioxide formed, Ryffel<sup>5</sup> has shown that lactic acid may be produced. Here, then, is an additional stimulus to the respiratory center. In an attempt to determine how great a pulmonary ventilation normal persons were capable of, a series of observations have been made in association with Mr. F. C. Hall and Miss B. I. Barker. The experiments consisted in having young men—doctors and medical students—ride on a stationary bicycle until they were forced to stop on account of shortness of breath. Some of the subjects were athletes in excellent training while others were accustomed to sedentary life. The subjects breathed through mouth-pieces and valves were used to separate the inspired from the expired air. The expired air was passed through a Bohr air meter and its volume measured for each half-minute of the time during which the subject was riding. The rate of the respiration was counted from a continuous pneumographic record. The data obtained over each half-minute consisted of the respiratory rate, the total volume of air breathed, and the average volume of each

<sup>3</sup> Arch. f. d. ges. Physiol., 1911, cxxxviii, 167.

<sup>4</sup> Biochem. Ztschr., 1913, xlii, 403.

<sup>5</sup> Barcroft: The Respiratory Function of the Blood, Cambridge, 1914, p. 239.

individual respiration. While there was a certain amount of variation among the different individuals in that some tended to greater increase of rate and others to greater increase of the depth of breathing, a number of interesting facts were elicited. Over the last minute and a half of the ride, thus when dyspnea was most marked, and just before having to stop, the minute-volume of air breathed ranged from 47.6 to 80 liters. The larger minute-volumes were, of course, in general found in the larger individuals. Comparing these figures with the minute-volume at complete rest it is found that these normal subjects could increase their pulmonary ventilation on an average of 10.7 times above the resting value. This gives a fairly accurate idea as to the great adaptability of the respiratory mechanism to any demands that may be put on it, and one has a quantitative value for what we may call the "pulmonary reserve." Since the high minute-volume depends on an ability to increase the rate and especially the depth, of respiration it is not surprising to find a close relation between the highest minute-volume and the vital capacity, or the volume of air which can be expired after the greatest possible inspiration. There is also a relation between the volume of the individual respiration and the vital capacity, and it is rather striking that the deepest respirations while riding averaged only 33 per cent. of the vital capacity. Curiously enough no definite differences were observed in regard to the respiratory mechanism between the trained and the untrained subjects. A point of considerable interest was the great difficulty experienced in making the subjects highly dyspneic, because they tended to stop riding on account of muscular fatigue rather than on account of shortness of breath. This was in part due to the fact that they were using muscles unaccustomed to heavy work, but it showed that in general the respiratory mechanism can normally adapt itself to any grade of metabolism that the body can produce.

Normally, then, "the pulmonary reserve" is so great, and the minute-volume of air breathed can be so easily raised to many times the volume at rest, that dyspnea is only noticeable under conditions of rather severe exertion. What, however, are the factors which tend to decrease the "pulmonary reserve" or to make a person more readily subject to dyspnea? What must one consider as possible elements in the cause of any pathological dyspnea? Since the "pulmonary reserve" depends on the relation between the minute-volume of air breathed at rest and the highest minute-volume which the subject is capable of breathing, it will be greatest if the minute-volume at rest is low. Thus, first among the factors which may cause an abnormal tendency to dyspnea are those conditions which produce a high minute-volume at rest. Chief among these are an increase of metabolism and the presence of an acidosis. Secondly, there are the factors which limit the ability of the subject to meet a demand for a higher pulmonary ventilation. Since an

increase in minute-volume depends on an increase of rate and depth of respiration, it is evident that a high initial respiratory rate, and more especially anything which interferes with deep breathing, will tend to reduce the pulmonary reserve. Finally, it will be seen that still other conditions probably underlie the type of dyspnea which is associated with periodic breathing.

From this point of view, then, we may approach the question of heart disease in an attempt to determine whether or not these possible factors are present, and in how far they may be considered as elements in the production of dyspnea. It is important to appreciate that dyspnea is one of the commonest symptoms met with in patients suffering from cardiac disorders, and that it appears in a considerable variety of clinical conditions. We shall therefore expect to find that the causes of dyspnea are not necessarily the same in different cases, and that while the symptom has a comparatively simple basis in certain instances, in others it is complex and depends on a number of interacting factors. The dyspnea which is noticed on ascending stairs by a subject with a compensated valvular lesion is quite a different thing from the continuous dyspnea of the same person when in a state of acute decompensation, and this in turn may have different underlying elements from the dyspnea of the patient with cardiorenal disease or the nocturnal attacks of paroxysmal dyspnea seen in an old man with chronic myocarditis.

Let us first consider the question of the metabolism in cardiac disease. The most satisfactory study of the basal metabolism in patients with heart disease was carried out at Bellevue Hospital, New York, in the calorimeter of the Russell Sage Institute of Pathology by Du Bois and Meyer in an investigation in which it was my privilege to take part.<sup>6</sup> Of fundamental importance was the demonstration by means of the close agreement between the methods of direct and indirect calorimetry, as well as by the finding of respiratory quotients which were within the normal limits, that the intermediary metabolism in heart disease follows a normal course. Sixteen patients were studied. The results showed that in compensated cardiac disease the metabolism is perfectly normal. Of 12 patients, on the other hand, who had some degree of dyspnea at the time they were studied 3 showed a normal metabolism and 9 a metabolism that was distinctly above normal. In 5 of the latter the metabolism was increased from 25 to 50 per cent. above the normal. The cause of the rise in metabolism is not evident. These and other more recent observations from the same source<sup>7</sup> indicate that it is not a necessary accompaniment of dyspnea, that it cannot be attributed to acidosis, and that it bears no definite relation to the level of the nitrogen in the blood. The subject has been further investigated in the medical laboratory of the Peter Bent Brigham

<sup>6</sup> Peabody, Meyer and Du Bois: *Arch. Int. Med.*, 1916, xvii, 980.

<sup>7</sup> Aub and Du Bois: *Arch. Int. Med.*, 1917, xix, Part 2.



Hospital<sup>8</sup> in association with Dr. J. A. Wentworth and Miss B. I. Barker. The indirect method of calorimetry was used, the apparatus consisting essentially of a large Tissot spirometer for the collection of the expired air and the Haldane portable gas analysis apparatus. By this method data are obtained regarding the *minute-volume* of air breathed which are lacking in the observations made with the large bed calorimeter. The results of the metabolism determinations in 24 instances agree essentially with those at the Sage Institute. They confirm the fact that in persons with mild grades of heart disease, in whom the lesion is comparatively well compensated, the metabolism is within normal limits, and they demonstrate again that in more severe cases, with or without dyspnea at the time of observation, the metabolism is variable, being frequently normal, but in some instances as much as 40 per cent. above normal. In only 2 cases was the heat production more than 25 per cent. above the normal, however, and, in general, the rise in basal metabolism is neither a constant nor a particularly significant feature. Of more immediate interest in the study of dyspnea are the observations on the minute-volume of air breathed. These show that while patients with mild cardiac lesions, and only a slight tendency to dyspnea, breathe a normal minute-volume of air, usually between 5 and 6 liters, the more severely affected patients who are either dyspneic while at rest, or who become so on very slight exertion, tend to have a considerably higher minute-volume. In this group of subjects the minute-volume at rest ran as high as 11.6 liters, while the average in 12 patients was 8.22 liters. There is, moreover, no definite relation between the minute-volume and the metabolism, and a high minute-volume may be found in a subject whose basal metabolism is wholly normal. A similar increase in the minute-volume has been reported by Beddard and Pembrey<sup>9</sup> and by other observers.

As to the cause of this increased minute-volume associated with a normal metabolism we have no absolute proof, but there is a very suggestive relationship between the raising of the minute-volume and the decrease of the vital capacity of the lungs. Practically all cardiac patients with a vital capacity of less than 60 per cent. of the normal (see below) show a high minute-volume, and a similar observation has been made in a case of pleural effusion. The decrease in the vital capacity of the lungs is probably associated with a lessening of the area of the respiratory surface, as, for instance, by the production of atelectasis by collections of fluid in the pleural cavity. The dead space, consisting of the nasopharynx, trachea, and bronchi, would not necessarily be affected and the resulting decrease in the respiratory surface, with a relative increase in the dead space, would bring about a rise in the actual minute-volume of air breathed

<sup>8</sup> Peabody, Wentworth and Barker: Arch. Int. Med., 1917, xx, 468.

<sup>9</sup> British Med. Jour., 1908, ii, 580.

in order that the alveolar ventilation, which is after all the essential thing, should remain constant.

In patients with severe manifestations of cardiac disease, then, an increase of the minute-volume of air breathed while at rest is very commonly present, whether or not there is any associated rise in the basal metabolism. In such cases the high initial minute-volume will be a factor in the production of dyspnea in that it limits the "pulmonary reserve." By diminishing the difference between the volume of air breathed at rest, and the maximum volume the subject is capable of breathing, it makes him more readily susceptible to the production of dyspnea.

Let us turn to the consideration of a second condition which causes an increase in the pulmonary ventilation, and which may thus act as a factor in the production of dyspnea in much the same manner as an increased metabolism. This is acidosis. The respiratory center is excessively sensitive to a shift in the reaction of the blood, and any considerable accumulation of acids in the blood stream causes a greater activity on the part of the lungs. Indeed, the production of hyperpnea is perhaps the most characteristic effect of acidosis.

In the recent enthusiastic attention which clinicians have accorded to the subject of acidosis the condition has been held responsible for a great variety of symptoms. It is not to be wondered at, then, that the relation of acidosis to dyspnea is a problem which has given rise to much conjecture and to a considerable amount of experimentation. Some observers, notably Lewis and his co-workers,<sup>10</sup> regard acidosis as one of the chief factors in the dyspnea seen in elderly persons with weak hearts and usually with kidney involvement—essentially the cardiorenal group. It is important therefore to examine in some detail into the conditions associated with cardiac disease in which acidosis is present and to consider in how far it may be regarded as responsible for the production of dyspnea.

As regards pure cardiac disease, one may state, as the result of many observations on the carbon dioxide content of the blood and alveolar air, that there is no evidence indicating the presence of an acidosis in compensated cases. In patients with pure cardiac disease in a state of acute decompensation the question is less simple to answer. Not infrequently the alveolar air analyses show a low carbon dioxide tension, while the blood analyses show a normal or high tension. With the regaining of compensation, and usually with the disappearance or continuous dyspnea, so that the patient is comfortable while at rest, the alveolar carbon dioxide rises quickly and the relation between the blood and the alveolar carbon dioxide becomes normal. How is this to be interpreted? It is possible that in these acutely sick persons the samples of alveolar air are not

<sup>10</sup> Lewis, Ryffel, Wolf, Cotton and Barcroft: *Heart*, 1913, v, 45.

reliable, but this explanation is hardly satisfactory, and it is much more likely that the condition is a real one. Peters,<sup>11</sup> who has studied the question at the Presbyterian Hospital, and who has found the carbon dioxide content of the blood considerably higher than that of the alveolar air, concludes, and most probably correctly, that there is an interference with the passage of carbon dioxide from the blood into the alveolar air. There is thus an accumulation of carbon dioxide in the blood and an acidosis in which an excess of carbon dioxide is the essential feature. The possibility of the presence of other abnormal acids due to incomplete oxidation, a condition similar to the acidosis of asphyxia, cannot be definitely excluded; but at any rate, in the production of dyspnea in pure cardiac disease, acidosis is a factor which only occurs in the most severely decompensated cases, and its influence in cases which recover is of short duration.

In cases of cardiac disease associated with renal insufficiency, on the other hand, the role played by acidosis is much more significant. Sellards<sup>12</sup> and Palmer and Henderson<sup>13</sup> showed the frequency with which acidosis occurs in chronic nephritis, and Straub and Schlayer<sup>14</sup> described the low alveolar carbon dioxide tension in uremia. Observations in our own laboratory have confirmed this work and helped to indicate the close relationship between acidosis and renal function.<sup>15</sup> In general, cases of chronic nephritis with a normal phthalein output show no signs of acidosis; with the failure to excrete phthalein satisfactorily an acidosis develops which shows itself by an increase in the "alkali-tolerance test;" and when the phthalein output has fallen to zero there is often a degree of acidosis sufficient to cause a fall in the carbon dioxide tension of the alveolar air. The recent work of Marriott and Howland<sup>16</sup> shows that the acidosis is due to the inability of the kidney to excrete acid phosphate.

A study of numerous cases of renal and cardiorenal disease shows that in the advanced stages, before and after the onset of uremia, and even just before death, the alveolar carbon dioxide tension is usually not below 25 mm. This is in itself not a sufficient drop to cause a marked hyperpnea. Indeed, in diabetes the increase in ventilation due to acidosis is not particularly noticeable until the carbon dioxide tension is approximately 15 mm. Considering therefore the comparatively mild grade of acidosis usually met with in chronic nephritis, one must hesitate to attribute to it too great a significance in the production of dyspnea. Occasional rare cases of nephritis present the clinical picture of coma and air hunger just before death and simulate diabetic coma. In these the carbon dioxide tension is

<sup>11</sup> Am. Jour. Physiol., 1917, xliii, 113.

<sup>12</sup> Bull. Johns Hopkins Hosp., 1912, xxiii, 289; *ibid.*, 1914, xxv, 141.

<sup>13</sup> Med. Communicat., Massachusetts Med. Soc., 1913, xxiv, 133.

<sup>14</sup> München. med. Wchnschr., 1912, lix, 569.

<sup>15</sup> Peabody: Arch. Int. Med., 1915, xvi, 955.

<sup>16</sup> Arch. Int. Med., 1916, xviii, 705.

about 10 mm., and the air hunger may be relieved by alkali. Thus in a very small group of cases the acidosis may be the direct cause of a hyperpnœa which is sufficient to produce dyspnea.

If, however, the acidosis which is commonly met with in chronic nephritis is not of itself intense enough to cause dyspnea it is by no means true that it is a factor to be ignored. Its significance may be made clear by some experiments carried on at the Peter Bent Brigham Hospital,<sup>17</sup> which were devised as a means of studying the production of dyspnea in normal subjects and in persons with cardiac disease. In order to avoid the dangers and difficulties attendant on the production of dyspnea in persons with heart disease by exercise, and to allow of the investigation of comparatively sick patients in bed, the dyspnea was produced by a continually increasing percentage of carbon dioxide in the inspired air. The subjects breathed through valves separating the inspired from the expired air. The expired air passed through a plethysmograph which was calibrated so that its movements, recorded on the smoked drum of a kymograph, gave an accurate index of the volume of each respiration as well as of the rate of respiration. The total ventilation for each minute could thus be calculated. After leaving the plethysmograph the expired air was rebreathed by the subject. The carbon dioxide tension of the inspired air rose progressively during the experiment and its percentage was determined by the analysis of samples taken at frequent intervals. As the result of a series of observations it was found that in normal individuals a given percentage of carbon dioxide produced a fairly constant rise in the pulmonary ventilation. Thus when the inspired air contained from 4.2 to 5.4 per cent. of carbon dioxide the minute-volume of air breathed was approximately twice what it was at the beginning of the experiment. Exactly the same relationship was observed in most patients with cardiac and renal disease. Their response to carbon dioxide fell into the normal limits. In a number of cases, however, in which the alveolar air showed evidence of an acidosis, abnormal findings were met with. Instead of the pulmonary ventilation being doubled by 4.2 to 5.4 per cent. carbon dioxide it became doubled when only 2 to 3 per cent. of carbon dioxide was breathed. In other words these patients were unusually sensitive to the stimulus of carbon dioxide and it required much less than normal to cause a considerable increase of the pulmonary ventilation. That this effect was actually dependent on the acidosis was demonstrated by performing the experiment again after enough alkali had been given to overcome the acidosis and to bring the carbon dioxide tension of the alveolar air back to its normal value. Under these circumstances the patients reacted just like normal subjects. The explanation of these results is simple. With the development of the acidosis the so-called "buffer action" of the blood becomes diminished and the addition to it of small amounts of carbon

<sup>17</sup> Peabody: Arch. Int. Med., 1915, xvi, 846.

dioxide which under normal circumstances would produce little change in reaction, causes enough shift in reaction to stimulate the respiratory center. It seems fair to conclude from these experiments that while the degree of acidosis which is commonly met with in patients with cardiorenal disease is not sufficient to cause any decided increase in the pulmonary ventilation, nevertheless, it may render the patients unusually susceptible to the production of dyspnea, and it is to be regarded as one factor in causing them to become short of breath on exertion. In severely decompensated cases, even the comparatively slight increase in the pulmonary ventilation while at rest may be sufficient to make the difference between comfort and discomfort in breathing. There is then a rational basis for the administration of alkali to patients with acidosis, and in certain cases definite relief of symptoms may be observed.

Having discussed briefly the two chief conditions which cause an increase of the pulmonary ventilation, let us now turn to the means by which the body responds to a demand for a higher minute-volume of respired air, and consider in what way these may be affected in heart disease. Such an increase in the minute-volume of air breathed is brought about by an increase of the rate or of the depth of breathing.

We may first give attention to the question of the depth of respiration and observe in how far a limitation in the capacity to breathe deeply is to be regarded as a factor in the production of dyspnea in heart disease. In the experiments just described in which the subjects were made dyspneic by rebreathing air containing increasing amounts of carbon dioxide, one striking difference was noted between the normal subjects and the patients who had cardiac disease.<sup>18</sup> While the former did not become extremely dyspneic until they were breathing from 60 to 80 liters of air per minute, the latter were forced to stop when they were breathing only 20 to 40 liters per minute. A study of the graphic records of the respiration during the experiments showed that this difference depended on the fact that the patients with cardiac disease were unable to increase the depth of their respiration as well as the normal subjects could. It is obvious that anything which prevents a person from breathing deeply is of profound importance as a factor in the production of dyspnea, for it immediately limits the extent to which the minute-volume can be raised, and this prevents him from meeting such increases of metabolism as he normally could. The inability to breathe deeply was found to correspond to a decrease in the vital capacity of the lungs.

It has long been known<sup>19</sup> that the vital capacity of the lungs is often decreased in heart disease, but no particular attention has been paid to the fact. It seemed, however, that the condition merited systematic investigation, and in association with Dr. J. A. Went-

<sup>18</sup> Peabody: *Arch. Int. Med.*, 1917, **xx**, 433.

<sup>19</sup> Arnold: *Ueber die Athmungsgrosse des Menschen*. Heidelberg, 1855.

worth a careful study of the subject has been made.<sup>20</sup> The vital capacity of the lungs is the volume of air that can be expired after the deepest possible inspiration. In our experiments the observations were made by having the subject breathe in and out as deeply as possible through a rubber mouth-piece connected with a calibrated recording spirometer. The movements of the spirometer were recorded on the smoked drum of a kymograph, and the vital capacity was determined by measuring the length of the line which corresponded to the greatest expiration and inspiration. In order to decide whether the vital capacity of any given patient was normal or not it was necessary to have standards for comparison, and since no wholly satisfactory data were at hand, observations were made on a considerable group of healthy persons. Ninety-six normal men and forty-four normal women were studied. It was found that standards which were sufficiently accurate could be established if the results were classified according to sex and according to height. Various other factors which influence the vital capacity of the lungs could be fairly neglected, as they were not particularly significant in the group of cases which we have studied. Thus old age causes a decrease in the vital capacity, but the majority of our patients were at a time of life when this did not play an important part. Athletic training increases the vital capacity, but this rarely affected our results, for in pathological cases it is the decrease that is significant. When placed in their appropriate groups according to sex and height it was found that 134 of the 140 normal subjects had a vital capacity of 90 per cent. or more of the normal figure.

Having thus established normal standards of the vital capacity of the lungs for men and women of different heights, it was possible to compare with them the results obtained in patients with heart disease. One hundred and twenty-four cases have been studied and about 224 records have been made. It is convenient to classify these patients according to the vital capacity into four groups, each of which presents rather definite clinical characteristics, and it will be seen that there is a very close relationship between the decrease in vital capacity and the tendency to dyspnea. Briefly summarized the results obtained are somewhat as follows:

Group.	Vital capacity, per cent.	Number of cases.	Mortality, per cent.	Symptoms of decompensation, per cent.	Working per cent.
I	90+	25	0	0	92
II	70 to 90	41	5	2?	54
III	40 to 70	67	17	39	7
IV	under 40	23	61	100	0

Certain cases were tested several times, and, owing to changes in the vital capacity, they appear in more than one group. In the "mortality" column they are included only in the lowest group into which they fell. "Symptoms of decompensation" indicates dyspnea while at rest in bed or on very slight exertion. Under "working" are included only those actually at work and able to continue. Many other patients in Group II were able to work, but they are not included, as they were still in the hospital.

<sup>20</sup> Peabody and Wentworth: *Arch. Int. Med.*, 1917, xx, 443.

Group I consists of 25 cardiac patients in whom the vital capacity was 90 per cent. or more of the normal standard. Thus in these cases the vital capacity does not fall below the limits found in healthy persons. All of them had well-compensated hearts, and dyspnea was scarcely a more prominent symptom in their histories than it would be found to be in a similar group of normal individuals. About 90 per cent. of them were working and the others were limited in their activities by cardiac pain or palpitation rather than by dyspnea. They were thus nearly all in extremely good general condition, and in many the cardiac lesion was merely an incidental finding. Group II consisted of 41 cases whose vital capacity was between 70 and 90 per cent. of the normal. These patients differed from those of the group with a higher vital capacity in that practically all gave a definite history of dyspnea on any unusual exertion. The majority, however, were able to work, and the rest, with two possible exceptions, could lead a satisfactory though somewhat restricted life. Several of them had passed through periods of more or less severe cardiac decompensation, and they are to be regarded as border-line cases whose activities must be somewhat limited, but who, under favorable circumstances, show little evidence of cardiac insufficiency. Group III consists of 67 patients in whom the vital capacity was between 40 and 70 per cent. of the normal. These cases are much more severely handicapped than are the members of Group II, and practically all suffer from dyspnea on moderate exertion. Those with a vital capacity only slightly above 40 per cent. are confined to bed or can do little more than get about the house, while those with a vital capacity approaching the upper limits can walk fairly easily, but they usually avoid the stairs or hills. Only 7 per cent. of this group were still at work. Attacks of severe cardiac decompensation occur with considerable frequency among these patients, and 17 per cent. of the number have died. Group IV consists of 23 cases with a vital capacity of 40 per cent. or less. All of them were severely decompensated and the majority were confined to bed. Dyspnea is either constantly present or it is produced by the slightest exertion. The prognosis for patients who fall into this group is bad. A few patients whose vital capacity has fallen as low as this during their first attack of decompensation have subsequently recovered so that they could lead a fairly active life, but most of them made comparatively little clinical improvement, and 61 per cent. have died.

These observations demonstrate the important role played by decrease of the vital capacity in the production of dyspnea in heart disease. In a surprisingly accurate manner the degree to which the vital capacity is decreased corresponds to the tendency to dyspnea. Patients who have no unusual tendency to become short of breath almost invariably have a normal vital capacity, and those who become dyspneic readily have a vital capacity which is depressed in accordance with the severity of the symptom.

But what, it may be asked, is the cause of the decrease of vital capacity in heart disease? The answer to this question is that there are many causes, some of which are obvious and easy to appreciate, while others still remain obscure. Anything which interferes with the free movements of the lungs, or the entrance of air into them, will decrease the vital capacity. Thus pleural effusions, fluid in the peritoneal cavity, emphysema, and pulmonary edema may be reckoned among the more gross conditions affecting it. These and other similar factors seem to explain the more severely decompensated cases, but there is a large group of patients with slight symptoms in whom the physical examination gives no clue to the reason for a decreased vital capacity. Further investigation into the cause of the decreased vital capacity in these subjects is clearly indicated, and the work of Siebeck<sup>21</sup> points to a promising line of approach. His comprehensive study of lung volumes in heart disease suggests that the low vital capacity depends on a change in the elasticity of the lungs which results from an engorgement of the pulmonary vessels due to back pressure from the left side of the heart. If this conception is correct, then the vital capacity of the lungs is an index of the state of the pulmonary circulation, and as such is of considerable clinical significance. It is probable that in many cases the earliest evidence of cardiac insufficiency occurs in the pulmonary circuit, but the usual methods of examination afford no means of detecting it. One clinical fact which is quite in accord with the theory that decrease in vital capacity with its attendant dyspnea is associated with a disturbance of circulation through the lungs is the common observation that dyspnea is an earlier symptom in disease of the mitral valves than it is in disease of the aortic valves.

If this relation between the vital capacity and the tendency to dyspnea is generally true when one compares a large series of cases with somewhat arbitrarily chosen normal standards, it becomes more so when one follows the individual patient and watches the changes in the vital capacity which are coincident with changes in the clinical condition. As long as the clinical picture remains constant the vital capacity is found to be the same, but when cardiac insufficiency becomes more marked and dyspnea more noticeable the vital capacity falls. Similarly, an improvement in the general condition and a lessening of the dyspnea is associated with a rise in the vital capacity. This parallelism is, indeed, so definite that the determination of the vital capacity seems to assume a practical significance. Dyspnea is, of course, only one symptom of heart disease, but it is a very common symptom, and it is an important one because the degree of dyspnea or of the tendency to dyspnea is a valuable index of the state of cardiac efficiency. The clinical records of cardiac patients abound with statements about dyspnea, but these

<sup>21</sup> *Deutsch. Arch. f. klin. Med.*, 1910, c, 204.



are always of limited worth, for they are based on either the history as given by the patient or on the gross examination of the physician. Dyspnea is, moreover, such a difficult condition to analyze or to describe that any objective method which allows one to obtain accurate quantitative information regarding it will serve a useful purpose. Such information the determination of the vital capacity appears to furnish even if only in a somewhat rough way. In many instances the observations have proved to give a more reliable conception of the clinical condition of the patient than has been obtained from either the history or the physical examination. This, of course, is true only in cases in which dyspnea is the presenting symptom, and does not hold for the group of patients whose cardiac lesion manifests itself by other symptoms such as pain or palpitation. However, the latter includes only a relatively small number of cardiac cases, and in a surprisingly large proportion of cases records of the vital capacity give important and helpful data as to the present status and the prognosis. They are often of much greater significance than are records of the pulse-rate or blood-pressure, and they seem to be a useful, although indirect, index of the cardiac reserve.

But, as we have already seen, the increase of the minute-volume of air breathed which accompanies a rise in metabolism is brought about not only by a greater depth of respiration but also by a higher rate of respiration. What, then, is the relation of rate of respiration to the problem of dyspnea in heart disease? The facts are simple and well known by all, so that the subject may be briefly dismissed. With the exception of the extremely mild cases of cardiac disease, which are in a good state of compensation, most instances have a respiration rate which is somewhat above normal, and the more severely affected the case the more rapid the respiration. Now there is, roughly speaking, a maximum rate to which the respiration can rise without losing much of its efficiency. The extraordinarily rapid breathing seen in some hysterical patients is, of course, economically wasteful. The maximum efficient respiratory rate will vary considerably in different individuals and under different circumstances, but it is interesting for purposes of comparison to note that the average highest rate of our normal bicycle riders was 34 per minute. Assuming some such figure as this for the high limit of efficient respiratory rate, it is obvious that the individual with a low initial rate while at rest has a marked advantage. The greater the difference between the rate of respiration at rest and the maximum rate of efficient respiration the greater is the reserve. With an initial rate of ten the respiration rate can be raised more than three times before the maximum of efficiency is reached, but with an initial rate of seventeen it can only be doubled. Thus the high rate of respiration which is found in severely affected cardiac patients is a significant factor in decreasing their reserve and increasing their tendency to dyspnea.

Having considered some of the general conditions which bear on the problem of dyspnea in heart disease we may now turn to a special type of respiration which deserves mention both because it is common in clinical practice and because its mechanism involves other considerations than those which have been as yet discussed. This is the periodic type of breathing which reaches its highest expression in the classical Cheyne-Stokes respiration. Careful observation, and more particularly the studying of records made with the pneumograph, impress one with the fact that the association of periodic breathing with heart disease is much more frequent than is generally recognized. It appears in cardiorenal cases, in aortic disease, and in advanced myocarditis, and it is most often characteristically seen in patients who suffer from attacks of nocturnal dyspnea. A history of the onset of dyspnea in the evening is often given by patients with myocardial weakness, and if they are watched it will usually be found that periods of dyspnea alternate with periods of apnea. During the apnea the patient dozes off and goes to sleep. With the beginning of respiration he arouses a little, and at the height of dyspnea he wakes up to find himself intensely uncomfortable and often gasping for breath. His discomfort disappears with the cessation of dyspnea, and during the period of apnea he falls asleep again. Such attacks are sometimes referred to as "cardiac asthma," but the name is singularly ill-chosen, for one of the most characteristic features of the true asthmatic attack is that the breathing is continuously rapid and labored. The volume of air expired has been measured in a few cases of mild periodic dyspnea, and the total minute-volume has not been found to be remarkably high. The chief difficulty, and the reason for the discomfort, appears to be that the patient is breathing only part of the time. The periods of apnea may last for half a minute, so that the patient is virtually breathing his minute-volume in the remaining thirty seconds. If he were to breathe the same minute-volume of air regularly over the whole minute much less discomfort would be experienced. The volume of the individual respirations rises to much above the normal, and since the vital capacity is usually decreased, the deepest respirations may approach the maximum of which the patient is capable.

What can one say as to the fundamental cause of this type of dyspnea? The question is unfortunately one which remains incompletely answered, but some facts have been gathered which throw light on it. The suggestion has been made that the attacks are associated with an acidosis. As opposed to this it is difficult to conceive of an acidosis of such sudden onset, and, moreover, the typical feature of the respiration in acidosis, such as that seen in advanced diabetes, is hyperpnea with deep regular breathing. The clinical picture is quite different from that of periodic breathing. However, to settle the problem more definitely Dr. F. T. H'Doubler has

studied the carbon dioxide content of the blood in a number of cases during the attack of dyspnea and either before or after it. Some of the patients who had advanced cardiorenal disease showed a slight decrease in the carbon dioxide tension, but this was rarely below 25 mm., and not sufficient to account for the dyspnea. Moreover there was no significant fall in the carbon dioxide tension during the attack of dyspnea as would be expected if the attack were dependent on a further increase in acidosis.

Douglas and Haldane<sup>22</sup> consider that the essential cause of Cheyne-Stokes respiration is oxygen lack, and they state that "the periodic breathing is produced by periodic occurrence and disappearance of the (indirect) excitatory effects of want of oxygen," which "may be due to abnormal deficiency in the alveolar oxygen pressure" or "to effects on the circulation of changes in the breathing or to both causes combined." This explanation accounted satisfactorily for the periodic breathing observed by them on the expedition to Pikes Peak.<sup>23</sup>

The frequency with which the attacks come on at night is a feature of interest. Periodic breathing is a normal phenomenon which occurs in many healthy persons during sleep and in hibernating animals. Straub<sup>24</sup> has shown that during sleep the alveolar carbon dioxide tension rises, and he attributes this to a decrease in the excitability of the respiratory center. Morphin, which depresses the respiratory center, often produces periodic breathing. May it not be that the periodic breathing in heart disease is associated with a change in the excitability of the center? In favor of this suggestion is its nocturnal occurrence, and the fact that in mild cases it often ceases if the patient is aroused or in any way excited. To test the question further, some observations have been made with Mr. F. C. Hall on the effect of caffein, a respiratory stimulant, on Cheyne-Stokes respiration. The number of cases as yet examined is comparatively small, but in nearly all a definite though very transient cessation of the periodicity of the breathing, often associated with subjective improvement, resulted from the administration of considerable doses of caffein. Several other drugs produced no noticeable effect. Morphin in the few instances studied caused no change or increased the periodicity, but its administration was therapeutically beneficial, for it depressed the central nervous system so that the patients did not arouse during the periods of dyspnea.

Whether Cheyne-Stokes respiration and periodic dyspnea in heart disease are due to oxygen lack in the sense of Douglas and Haldane or to a depression of the excitability of the respiratory center,

<sup>22</sup> Jour. Physiol., 1909, xxxviii, 40.

<sup>23</sup> Douglas, Haldane, Henderson and Schneider: Tr. Royal Soc., London, 1912, cciii, Series B, 185.

<sup>24</sup> Deutsch. Arch. f. klin. Med., 1915, cxvii, 397.

or possibly to a combination of the two, is a problem which still awaits solution.

Such, then, are at least some of the factors which contribute to the cause of that common but singularly complex symptom of heart disease—dyspnea. In its final analysis the problem resolves itself into the question of what we have called the “pulmonary reserve.” The degree to which any individual manifests a tendency to dyspnea depends on the relation between the volume of air which he breathes while at rest and the maximum volume which he is capable of breathing. The ability to meet adequately the needs of an increased metabolism, such as occurs with muscular exercise, depends on the “pulmonary reserve.” In normal persons, as has been seen, the “pulmonary reserve” is great, and healthy young men can increase their pulmonary ventilation to approximately ten times the volume required by their resting metabolism. But in patients with heart disease the circumstances are much less favorable, and various conditions arise which cut down the “pulmonary reserve” and make them more readily subject to dyspnea. An increase of metabolism, or the development of an acidosis may raise the volume of air breathed while at rest, while an increased respiratory rate or a decrease of the vital capacity of the lungs will make the maximum ventilation of which they are capable much lower than the normal. A decrease of the “pulmonary reserve” results, and even moderate exertion causes a rise of metabolism and a pulmonary ventilation which produces the subjective sensation of dyspnea. The degree to which these different factors are present in any given case is extremely variable. The earliest and most constant feature in the production of dyspnea is apparently a fall in the vital capacity, and it is often met with quite unaccompanied by any of the other factors which we have considered. In advanced cases of cardiac disease the situation becomes much more complicated. The vital capacity drops still lower, the rate of respiration rises, the metabolism increases, and an acidosis may appear. Finally, the picture is still farther confused by the onset of periodic respiration, and it becomes indeed, quite impossible to determine which element is most responsible for the patient's unhappy state.

Our conception of the etiology of dyspnea in heart disease is still vague and incomplete. Some little insight we have obtained, but further knowledge must come from the careful investigation of the individual case, the discovery of other factors in the cause of dyspnea, and the systematic grouping of the separate types of dyspnea. Only by such studies can we hope to reach our ultimate aim—the proper treatment and the relief of dyspnea in heart disease.

# WAR MEDICINE

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**The Scabies Problem on Active Service.**—MACCORMAC and SMALL (*British Med. Jour.*, September 22, 1917). Diseases of the skin are very important from the point of view of military efficiency, for they occupy one of the premier positions in producing "casualties." Under the conditions of trench warfare they prevail very widely, and since many are contagious, preventive measures are highly important. Next to pediculosis, scabies is the commonest skin disease met with among soldiers. Under the hard conditions of active service, secondary pyodermic complications are frequent and severe and cause prolonged sickness. While simple, uncomplicated cases are cured in three or four days, those with pyodermic complications are incapacitated from duty, and in a large series of cases observed the average stay in hospital was one month. The primary disease is often marked by these complications, such as impetigo, furunculosis, dermatitis, and inguinal adenitis, and in all cases of these, scabies must be carefully looked for. The characteristic interdigital burrows are found much less frequently than in civil practice, and indeed there is often complete absence of all lesions from the hands. In the majority of cases the penis is involved and the discovery of papules or crusts is almost pathognomonic. In addition to the associated pyodermic complications and

pediculosis, the condition must also be diagnosed from pompholyx, venereal disease, and an unusual papular urticaria. All the evidence points to blankets as being the chief means of disseminating infection. Blankets should, therefore, be sterilized as often as possible. Infected men should be segregated and treated as soon as possible. To discover the infection before it spreads, regular medical inspection is necessary. A few cases seem to be contracted from horses, and therefore these must also be inspected. Treatment is by simple inunction with sulphur ointment, and good results are invariably attained, if the treatment is conscientiously carried out and with due regard to the necessary details. These the authors give in outline. They condemn the unreliable sulphur vapor method, which was discredited a hundred years ago, but which has been revived again.

### RECALLED TO LIFE.<sup>1</sup>

A JOURNAL DEVOTED TO THE CARE, RE-EDUCATION, AND RETURN TO CIVIL LIFE OF DISABLED SAILORS AND SOLDIERS.

No. 1.

Pages 1-199

- I. Introductory.
- II. Treatment of the Disabled: being a Memorandum prepared by Sir Alfred Keogh, G.C.B., for the Anglo-Belgian Committee.
- III. Address to Allied Conference. By Lieut.-Colonel Sir Arthur Boscawen, M.P.
- IV. Orthopedic Surgery in its Relation to the War. By Colonel Sir Robert Jones, C.B.
- V. A Talk with the Disabled.
- VI. Miscellanea.
- VII. Pensions. By Captain Basil Williams.
- VIII. Work in France and Germany.
- IX. Notes.  
Facilities for Special Treatment.  
Training Classes for the Disabled.

#### I. INTRODUCTORY.

It is here set forth that:

"It is the purpose of this Journal to diffuse as widely as possible among those who are in any way concerned with the welfare of our sailors and soldiers returning disabled from the war, and not less among such sailors and soldiers themselves, knowledge as to the means by which they may be restored, as nearly as the nature of their injuries permits, to full participation in, and full enjoyment of, the activities of civil life."

Then follows a brief consideration of some of the broadly social conditions to be met in this effort and the introduction concludes with the following:

"The organization now in being for training the disabled man, for opening to him a satisfactory place in life, and incidentally

<sup>1</sup> Published by John Bale, Sons & Danielsson, Ltd., Oxford House, 83-91, Great Titchfield Street, Oxford Street, W. I., London. Editor, Lord Charnwood; Assistant Editor, Everard Cotes.

for carrying his cure farther, is not complete, but for some time past it has been far more effective than is commonly known. The subject is large and is intricate. It is hoped that succeeding numbers of this Journal will be able to present something like a complete map of the field, and thereafter a continuous and inspiring record of the work that is being done in it."

## II. TREATMENT OF THE DISABLED.

This article will appear to most readers as a more comprehensive *résumé* of the subject than the sub-title, "Memorandum" would imply. It begins with a consideration of the origin of such agencies as now exist, dating from the appointment of a Government Committee under the presidency of Sir George Murray, G.C.V., shortly after the outbreak of the war, and extending down to the present day. The question of pensions is then touched on at some length and the balance of the article is devoted to consideration of the actual measures instituted and the means by which they are made possible. The scope of this general program and the thoroughness with which it is carried out is illustrated by the following outline:

"In accordance with the provisions thus set forth, the history of a sick or wounded man who has been declared to be unfit for further military service may be given as follows:

"(1) He is brought to a first-grade hospital in the United Kingdom for treatment by specially selected physicians and surgeons.

"(2) He is transferred to an auxiliary hospital for continuance of treatment during his convalescence.

"(3) He is returned to a first-grade hospital and is, in due time, brought before a board of Royal Army Medical Corps officers, who testify, in the appropriate documents, as to his condition, the origin of his disability, etc., for the information of the Pensions Ministry. He is visited by representatives of the Local Committee of the area in which the hospital is situated and, by them, appropriate information regarding his condition and circumstances is conveyed to the Local Committee of the area in which he is going to reside.

"(4) When about to be discharged from hospital to his home, he is given a card, containing essential information, which he keeps. A similar card is sent to the Local Committee of his home area by the hospital authorities.

"(5) On arrival at his home he is visited, or communicated with, by a representative of his Local Committee and informed of arrangements which have been made:

"(a) For his treatment (if any);

"(b) For his reëducation (if required);

"(c) For his employment (if necessary);

"(6) Meanwhile he is receiving a pension, the amount of which depends upon the gravity of his disease or injury, and this pension may be supplemented, the amount of such supplementary aid depending upon the various circumstances of the man.

"(7) If his is an orthopedic case he is treated at an orthopedic hospital; if his is an ordinary medical or surgical case, either by

a general practitioner or by attendance at any general, civil, or military hospital.

"(8) During this period of out-patient treatment he undergoes the process of reëducation, in so far as he is physically fit, and at the termination of the treatment his whole time is available for reëducation.

"It will thus be seen that, whether we consider the subject from the point of view of the State or of the individual, the several indications which the situation requires to be fulfilled, are met. The State provides that the maimed soldier will be retained in hospital so long as he requires in-patient treatment, and that on discharge there is a great civil organization ready to receive him, to continue his treatment, to reëducate him and to provide for his employment. The man is under no anxiety as to the well-being of his dependents during this preparatory period. He is not driven by necessity to return prematurely to a calling in civil life before his treatment is fully completed. When he is in the hands of the great civil and military hospitals he has the best medical and surgical advice which the country can provide. If he lives at a distance from an appropriate hospital he can be brought to live in the neighborhood of one, or proceed there daily from his home. The State maintains him throughout all these processes, and a pension is provided on a scale already set forth."

### III. ADDRESS TO ALLIED CONFERENCE.

Some attention is given to the Inter-Allied Conference for the study of the problems relating to the disabled soldiers throwing light on the work shops and other agencies through which the men acquire added function. The article is well illustrated with photographs showing men with various types of disability, engaged in a large variety of occupations not only after training but also during convalescence. Perusal will well repay those who are interested in this general subject, since it reveals how much has already been accomplished in this connection in England and elsewhere and what this country will be called upon to do in the future.

### IV. ORTHOPEDIC SURGERY IN ITS RELATION TO THE WAR.

Under this heading Colonel Sir Robert Jones discusses briefly the leading problems to be met in this increasingly important field, his view-point being not alone that of the orthopedist, but including also consideration of the individual, his psychic condition and the necessity of frequent consultations with other departments of medicine, in order to achieve a well-rounded result, and not merely a mechanical improvement.

### VIII. WORK IN FRANCE AND GERMANY.

One of the leading articles of the Journal is an epitome of the efforts in France and Germany toward the rehabilitation of the wounded and is in the nature of conclusions, following a previous report from the Intelligence Department of the local Government Board (England). It is largely a statistical report, and contains much information essential to those seriously interested in this field.

R. P.



## I. Recent Developments

(a) The Pensions Ministry, by Lieut.-Col. Sir Arthur Griffith-Boscawen, J. P., M. P.; (b) The War Office, by Colonel Sir Walter Lawrence, Bart., G. C. I. E., C. B.; (c) The British Red Cross Society, by the Hon. Sir Arthur Stanley, G. B. E., C. V. O., C. B., M. P.

II. A General Survey. By the Editor.

III. Disablement in the Royal Navy. By Fleet-Surgeon P. Hamilton Boyden, M.D., R.N.

IV. The Labor Party and the Disabled. By G. J. Wardle, M. P.

V. Neurasthenia and Allied Disorders. By Col. Sir John Collie, M.D., A.M.S.

VI. Tuberculosis. By Major P. Horton-Smith Hartly, M.D., C.V.O.

VII. The Problem of the Crippled. By Sir William Osler, Bt., F. R. S.

VIII. Work in the Overseas Dominions and India.

IX. Committee on Institutional Treatment.

X. The Disabled Canadian Soldier.

XI. Miscellanea.

XII. Correspondence.

XIII. Notes.

XIV. Facilities for Treatment and Training.

## I. RECENT DEVELOPMENTS.

Under this heading in a joint article by several contributors, a few pages are devoted to the arrangements in progress or recently completed under the Ministry of Pensions, the War Office and the British Red Cross Society, toward the care, reëducation and return to civil life of the disabled. Perhaps the most significant statement is by Col. Lawrence, who says:

"It is believed by many that orthopedic treatment will become a part of the national life. . . .

"But whether orthopedic centers become permanent institutions or not, it is obvious that they will be required for many years after the declaration of peace, and it behooves the State to take early measures to secure their permanency when the War Office ceases to be responsible. The orthopedic problem concerns over one-third of our wounded men. It is a grave problem now; it will be graver when peace is declared."

## II. GENERAL SURVEY.

This is a survey on the part of the editor as to the different forms which disablement takes and the different needs which arise in each case; as to the actual extent to which provision for these needs is lacking or incomplete or relatively complete; as to the practical issues involved in controversies on this matter; and as to the functions of different authorities and institutions in regard to disabled men.

One of the most interesting features of this article is a table setting forth the proportion of injuries and diseases among every thousand disabled men, excluding officers, so far discharged from the English Navy or Army during the war.

## CAUSE OF DISABLEMENT.

Injury to eyes (including an occasional case of total blindness)	32
Amputation of leg . . . . .	30
Amputation of arm . . . . .	19
Injury to leg not requiring amputation . . . . .	122
Injury to arm not requiring amputation . . . . .	82
Injury to hand not requiring amputation of whole hand . . . . .	61
Injury to head (including say six or seven paraplegic cases) . . . . .	47
Hernia . . . . .	7
Miscellaneous wounds and injuries (including, say, about five paraplegic cases) . . . . .	53
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Total wounds and injuries . . . . .	453
Diseases of chest (including, say, 60 tubercular cases) . . . . .	124
Rheumatism . . . . .	50
Diseases of heart . . . . .	110
Epilepsy . . . . .	11
Nervous cases . . . . .	47
Insanity . . . . .	9
Deafness (partial or, in comparatively rare cases, total) . . . . .	26
Frost-bite (including cases of amputation, which are less than one-tenth of the whole) . . . . .	10
Miscellaneous diseases (among which may be noted, beside a few paraplegic cases, Bright's disease, ulcer of stomach, debility and varicose veins) . . . . .	160
<hr/>	
Total cases of disease . . . . .	547
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	1000

Apropos of these figures the writer remarks:

"A further glance at our table, in the light of what has just been said, will suggest what a knowledge of the total numbers discharged and awaiting discharge through loss of a limb would confirm, that the number of men lying under this misfortune will certainly never exceed the number which the community can easily absorb and place, if they themselves so will, in honorable and relatively assured occupations. That it is well within the compass of our powers to honor this debt, is but an additional incentive to doing so."

The article concludes with a censure of those who criticise the apparent inability to meet the problems of the disabled which is suggested by the sight of the afflicted. The author remarks that the machinery is there to help the men, and makes the point that critics should bestir themselves to have a particular case rightly treated, with the means already at hand, before attempting to reform the general system.

#### V. NEURASTHENIA AND ALLIED DISORDERS—THE MANAGEMENT OF NEURASTHENIA.

This is a very broadminded and dispassionate consideration of the large subject of neurasthenia. It is interesting to note the following general summary of the main symptoms which present. In the author's words;

"I have found, from consideration of a large number of consecutive cases, that the following are the most common symptoms: Disorderly action of the heart, epileptiform seizures, tremors, functional stiffness and functional loss of power of muscles, loss of flesh, and loss of hearing and speech. From the mental or emotional side, we have subjective symptoms which, although sometimes intangible, are very real to the patient, such as mental lassitude, giddiness, nightmares, loss of self-control and confidence, loss of power of concentration and fear of closed or open spaces, nervousness, a vague feeling of apprehension, and, in the more acute stages, confusion of thought."

The writer places great emphasis upon the fact that neurasthenia under these conditions is not a fraud or a self-deception but a very real disease, found frequently among men remarkable for their bravery and initiative.

Most of the neurasthenics encountered by the writer were suffering from shock caused by high explosives and have had some commotion of the nervous system; but before going under medical care in England they have generally recovered from the grosser pathological conditions and present chiefly mental and emotional phenomena. No short-cut in treatment is suggested but, on the contrary, great emphasis is laid upon the importance of the consideration of every case individually, upon its own merits and the institution of those well-recognized conditions and methods which form the underlying bases of health, such as fresh air; wholesome food; light graduated work, together with such adjuncts as massage, electricity and the like.

The writer emphasizes the fact that psycho-therapeutic methods of treatment have been found to be wonderfully effective provided they are in the right hands. He adds that nothing in the nature of so-called psycho-analysis is necessary, however, and regards it as sufficient for the physician to find out what is worrying the patient and what is keeping him from getting well, which, he says, can be achieved without psycho-analysis. In his experience patients do best if isolated for a short period during the earlier part of the treatment, provided this is not interpreted as "solitary confinement." They thereby become more susceptible to the suggestion of rapid recovery, which is the frequently emphasized aim of the physicians and nurses. The writer also pertinently remarks that unless the patient desires to get well no treatment can cure him, and furthermore places great emphasis upon work in one form or another as the only salvation for those suffering from functional nerve disease. Among the most interesting and striking principles which form the basis of Colonel Collie's methods are the facts that he demands optimism and enthusiasm in all co-workers associated in such efforts; that any patient making no progress should be sent elsewhere for treatment and that in order to maintain the proper atmosphere and general level of effort among doctors and nurses, no one should be overworked. He feels that the issue cannot be forced in this connection and that attempts to do so defeat themselves.

## VI. TUBERCULOSIS.

Tuberculosis is considered under the general heading of Early Cases, Advanced Cases and Farm Colonies. No attempt is made to take up the details of treatment, but rather there are pointed out the various

social relations which assume importance in connection with this problem and the means of turning them to advantage when possible, such as utilizing mild out-of-door activities where indicated and returning the healed tuberculous to their own previous occupations under conditions of lessened strain.

#### VII. THE PROBLEM OF THE CRIPPLED.

Sir William Osler has contributed two pages to a bird's eye view of this question and calls attention to the fact that whereas the term "orthopedie" was originally confined to the familiar narrow meaning, it has now grown to include relief for deformities and disabilities of all kinds. Dr. Osler remarks:

"All of us really needed this art—some in minds, others in bodies, many in both! In a sense, education is a department of orthopedies. This branch of surgery has grown in a remarkable way within the past twenty-five years. There are general surgeons I know who do good orthopedie work, but the new orthopedies is more than surgery. The orthopedie surgeon is a teacher, a personal teacher, and in two directions—of the patient's mind quite as much as of his muscles and joints."

In conclusion he says in the last paragraph:

"And there is another side to this problem. Plato tells of a friend whose ill-health had kept him out of the hurly-burly of public life to the great benefit of his mind. This 'bridle of the ages,' as he calls it, may have a real value. A physical burden bravely borne makes a strong man, whose moral force in a community is worth a score of mere men-machines." R. P.

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**War Nephritis.**—SUNDELL and NANKIVELL (*Lancet*, September 15, 1917) come to the tentative conclusion that war nephritis may be attributed to some error in metabolism due to dietary insufficiency. The report is based on 250 clinical cases. Laboratory tests were made on the urine of the last 50 of these. In the 250 cases there were 7 deaths. Postmortem examinations were made, but owing to the absence of laboratory facilities in only 1 case was microscopic investigation possible. There are all gradations of severity of the disease, ranging from the slight attack with little or no edema to the typical and fatal case. In every typical case are seen edema, dyspnea, and headache. The edema always affects the face, and, in addition, in order of frequency, feet, hands, lumbar region, scrotum, and abdominal wall. Other symptoms often met with, but not invariable, are backache, limb pains, slight pyrexia, and scanty micturition. Some degree of respiratory distress is constant. Most of the patients describe the onset as quite sudden; the man may parade in full marching order without discomfort and fall out a few minutes later, quite unable to march after the column has gone a few hundred yards. Many of the men, however, when closely questioned, state that they had noticed gradually increasing shortness of breath for two or three days before the dramatic attack. In a large proportion of cases the dyspnea precedes the appearance of facial edema by several days. At the beginning, oliguria, or suppression of the urine, is the rule, followed after a few days frequently by polyuria. Albuminuria is constant at first, but may be remarkably transient. Blood in the urine could

be detected with the naked eye in a little less than half the cases. The only two serious complications are bronchitis and uremia. The presence of the former has a very adverse influence upon the prognosis. Uremia is seen in about 8 per cent. of the cases. Its onset is usually early, and indeed it may be the first manifestation. The common manifestations of uremia are torpor, severe headache, nausea, vomiting, and convulsions. The convulsions occur with very little warning, and are very violent. These convulsions, if not immediately fatal, were found to be apparently of good prognosis, inasmuch as several patients made a rapid and almost complete recovery after having had severe convulsions. In the examination of the urines it was found that all cases of war nephritis showed casts, most commonly of the hyaline and granular varieties. Also, all cases showed the presence of degenerate endothelial cells. The authors regard the presence of the casts and the endothelial cells as sufficient microscopic evidence on which to diagnose this form of nephritis. The endothelial cells were found to persist in the urine after the casts have disappeared, when the patient was apparently well; 36 out of 50 cases showed red blood corpuscles in the urine, but the amount of blood did not appear to indicate the severity of the attack; 22 had albuminuria. At autopsy gross examination of the kidneys showed very little departure from the normal. Microscopic examination of the kidneys from one case showed the nephritis to be focal and not diffuse, healthy areas and diseased areas intermingled. In the latter both tubules and glomeruli were affected. Various hypotheses have been advanced as to the cause of the condition, such as damp, cold, and exposure, or fatigue from forced marches. These and others are detailed, but the authors consider that the number of causes suggested shows that the real cause is probably still unknown. However, the fact that officers and the Indian troops were comparatively immune seems significant to them. These both had a certain amount of fresh food which the other soldiers did not. The officers supplemented their canned rations by buying fresh food, while the Indian troops received fresh meat newly killed and fresh milk, not the tinned variety. The other soldiers lived practically on canned or frozen meat and condensed milk. To this diet the authors are inclined to place the cause of the war nephritis.

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**Trench Fever Associated with the Presence of a Hemogregarina.**—**DIMOND** (*Lancet*, September 8, 1917) announces the discovery of the presence of a small hemogregarina in the venous blood and in blood from liver, spleen, and lung punctures of a series of 12 cases of trench fever, and has further confirmed the finding in a number of cases which he has seen more recently. Study of capillary blood failed to give uniform results, so that venous blood had to be used. The organisms were found in but small numbers, even when the blood was examined upon the day or two preceding the febrile stages of the disease. The methods are given of showing up the organism and of studying its movements on the warm stage. The action of trypan red and allied substances upon the organism was watched under the microscope. In certain dilutions of trypan red there appears to be a definite slowing and even cessation of the characteristic movements

of the parasite. This is also the case when trypan blue and trypan-flavine are used. These dyes are being tried clinically, and already good results are shown by the use of the trypan-flavine. The cycle of development of the protozoan was studied on blood and cells derived from liver, spleen, and lung punctures. The liver appears to be the main habitat, as well as the spleen and lung, and probably bone marrow. The author believes that spleen puncture is the quickest way to make a diagnosis of trench fever. What carries the infection is undetermined, but it is suggested that the pediculus corporis or perhaps a louse parasite on rats is the agent. The close relationship of the rats and men in the trenches is in favor of this suggestion. The stomach cells of the various kinds of lice found upon the underclothing of the soldiers are at present being examined.

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**Some Statistical Results of the Treatment of Chest Wounds.**—ELLIOTT (*Lancet*, September 8, 1917). The after-history of 170 cases of chest wounds are first considered. These patients had been transferred from France usually in the third week after the wound had been received, or a week or two later if an empyema had been drained by rib resection. The mortality from such wounds is being variously estimated at the present time, but it is certain that all deaths occur in the first month. If this period of time is survived the injury is neither of a fatal nor necessarily of a disabling character. A chest wound may invalid a soldier for two or three months if it is simple, or for any time up to a year if it has been accompanied by a large or by an infected effusion into the pleural cavity. But the ultimate recovery is very good, and few of the survivors of such wounds need to be invalided out of the army. The periods of invalidism are considered with reference to the occurrence of a sterile hemothorax, of empyema, of pneumothorax, and of lung laceration. In all the 170 cases whose histories were followed, it was very rare for any further surgical intervention to be found necessary. There was but one death, and that from an operation, undertaken at the patient's request, for the removal of a bullet. There was, in no case, any fresh effusion that required aspiration. Retained foreign bodies were seldom interfered with, and apparently caused no further trouble. Most lung wounds are accompanied by laceration of greater or less degree, but the evidence from the cases followed seems to show that laceration of the lung tissues are very readily repaired. Scar tissue quickly closes up the defect, and pneumonic inflammation or gangrene does not spread from the neighborhood of the track. A sterile hemothorax of moderate size, about 30 ounces, which does not cause much cardiac displacement, need not be aspirated. In the case of larger effusions, those which were aspirated gave tolerably good results, at least 30 per cent. of them being well again within three months. When such cases remained unaspirated, the late results have been described as being most unsatisfactory, the lung remaining collapsed and the chest expanding very poorly. The retention of foreign bodies in the chest in aseptic cases does not seem to affect recovery, but more extended information is urgently needed on this point. In cases of septic hemothorax, which had been drained in France and transferred to the United Kingdom, the period of convalescence is determined by the size of the cavity and by the nature of

the collapse of the lung and the thickness of the fibrin coat overlying it. Much depends on the proper placing of the original drainage opening and a satisfactory removal of carious ribs. It is certain too that systematic breathing exercises combined with antiseptic lavage of the cavity will hasten the closure of the sinus. In empyemata the retention of a shell fragment or other foreign body was seen to have an unfavorable influence on the possibility of the soldier's return to duty, and at least one-third of the empyema cases had ultimately to be discharged from military service as unfit simply on account of the chest condition. The mortality from chest wounds in France are also considered. It has been fully demonstrated that thoracic operations are quite practicable under military conditions in the field. It has been found that the pleural cavity may be freely opened under ordinary local or general anesthesia and the lung manipulated without any fear of immediate physiological disturbances. It is essential that infection shall neither be spread broadcast nor introduced by drainage of the pleural cavity at the end of the operation. However, although the results are often striking they are not always favorable, and comparison by statistics will need to be made with the results of the older more conservative treatment in order to see which kind of chest wounds are best suited for treatment by the new methods. Deaths after chest wounds are caused either by primary hemorrhage or by infection in the chest. All deaths occurring on the first day may be ascribed to the former, while all deaths from the second day onward are due to the latter. Sepsis is twice as frequent with wounds by shell fragments as with those by rifle bullets. About 10 to 15 per cent. die at an early date from the severity of the wound and about 10 per cent. may die later at the evacuation hospital from complicating sepsis. Among those cases developing sepsis within the chest the mortality is very high, rising to nearly 50 per cent. under the present treatment by rib resection and drainage. The old conservative routine of surgical non-intervention, except by late drainage, shows good results in those cases of gunshot wounds of the chest which remain non-infected—that is about 75 per cent. But the septic cases demand the newer practice of prophylactic cleansing operations, performed at an early hour, on certain carefully chosen groups of cases.

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**Psychological Examining in the Army.**—MAJOR M. YERKES, Sanitary Corps, National Army, Section of Psychology, Office of the Surgeon-General says the Medical Department of the Army has undertaken to test thoroughly the military serviceableness of certain methods of psychological examining. This is being done in accordance with carefully formulated plans in four National Army cantonments (Camp Devens, Dix, Lee, and Zachary Taylor) and in one Officers' Training Camp. The methods which are being applied were especially prepared for use in the Army by a Subcommittee of the National Research Council. In order that all enlisted men might be examined expeditiously a procedure suitable for the examining of groups was devised. This permits a single examiner to make measurements simultaneously of the intelligence of from 100 to 200 men. In briefest outline the handling of men by organizations is as follows: A company is reported at a given place for psychological examination. If its strength does not

exceed the capacity of the examining room it is taken as a unit and settled for examination. The first step is to divide the organization into two special groups, the one of which consists of men who are capable of reading and writing English fairly well, the other of those uneducated or foreign-born individuals who are not able to read and write English satisfactorily. This segregation of the original group or company is accomplished by means of a simple literacy test. As soon as this initial test is completed the group of illiterates is ordered to another examining room, where a form of group examination suitable to those who have but slight knowledge of English is given. The group of literate subjects proceeds in the original examining room with a special examination for the measurement of intelligence. In neither of the group examinations is any considerable amount of writing demanded. The aim is rather to obtain reliable indications of the ability of individuals to respond to different types of situation by having them make relatively simple movements, such, for example, as under-scoring or crossing out words, making crosses in the proper places, constructing simple objects, reproducing or completing diagrams and other figures and so on. The principal purposes of psychological examining in the Army are: (1) To discover those men who by reason of intellectual deficiency or peculiarity of mental constitution are either unfit or undesirable for military service. (2) To supply a practically reliable intelligence rating or rank for every enlisted man which shall assist his Company Commander in placing him wisely and using him effectively for military purposes. (3) To supply mental measurements which shall be of value in connection with the selection of men for non-commissioned or commissioned appointments and for special lines of skilled service. Psychological examining has been in progress since early in October. Up to December 1 approximately 60,000 enlisted men of the National Army, 4000 commissioned officers, and 1000 candidates for appointment in an Officers' Training Camp had been examined and the results reported to the proper medical officer, company commander, or commanding general of the division. Among the enlisted men from 5 to 10 per cent., varying with organization and race, were reported as intellectually very inferior. Of this number from 1 to 2 per cent. were designated as cases of mental deficiency whose discharge from the army seemed eminently desirable. For each company examined, report of intelligence ratings was immediately supplied to the company commander. Official reports indicate that this psychological information has been of service to many officers in connection with the training of their organizations. Repeatedly commanding officers on receiving psychological reports have requested the special and individual examining of certain men who, because of disorderly conduct or inability to learn, have proved themselves to be difficult problems. The examining of officers or of candidates for appointment has yielded results which correlate most satisfactorily with the expert opinion of military men. Certain organizations have already made use of intelligence ratings as an aid in equalizing the strength of the commissioned personnel of their various subdivisions. Everything indicates that psychological examining as at present conducted in the Army has strictly military as well as medical reference and significance. Its results can be used alike effectively to strengthen



organizations by ridding them of unsuitable material and by placing individuals, and especially those of superior ability, where they can be of greatest service. It is clear from this preliminary trial of psychological examining that the organizing of military groups should rest upon adequate knowledge of the mental characteristics of individuals as well as on like knowledge of their physical qualifications and military training or experience.

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**Public Health and Control of the Liquor Traffic.**—LORD D'ABERON (*Jour. State Med.*, 1917, xxv, 321), who is Chairman of the Central Control Board (Liquor Traffic), suggests in the opening remarks of his address that health officers have not given as much attention to this subject as it deserves. It is true that it is only quite recently that health officers have taken action in relation to the control of alcoholism, though it has not been from lack of appreciation of its importance, but rather from a well-founded fear that active warfare against the unscrupulous liquor interests would end disastrously for public health. Health officers, as have most medical men, tried by every means to educate the public to an appreciation of the evils of alcohol. They have usually and wisely refrained from taking an active part in securing restrictive or prohibitive legislation. Lord d'Aberon believes that the discouragement to the use of distilled liquors and the shortening of the hours of sale have had a marked effect in decreasing drunkenness and other alcoholic diseases. He gives figures for each of the four years, 1913-1916. In 1914 there was no restriction, but the laws went into effect midway in 1915. The comparison is best made, then, between 1914 and 1916. The deaths from all diseases in England and Wales connected with alcoholism decreased 43.9 per cent. (for males 41.5 and for females 47.1). The decrease for cirrhosis of the liver (not certified as alcoholic) was 23.1 per cent. (for males 17.1 and for females 31). It was admitted that a part of the decrease for males might be due to the absence of so many men at the front, but the speaker said that most of the deaths from alcoholism are of persons over forty years of age and that few chronic alcoholics are accepted for service. Naturally, a chronic process, like cirrhosis of the liver, is less affected than are acute manifestations. Figures from Liverpool were presented as of particular value, as the mortality figures were secured from Dr. Hope, the distinguished health officer of that city. The deaths from delirium tremens in Liverpool decreased during the time mentioned above from 366 to 128 for males and from 145 to 77 for females. Other forms of death from excessive drinking fell from 85 to 35 for males and from 41 to 14 for females. At the same time arrests for drunkenness fell from 13,201 to 6,277. The speaker had no doubts that the restrictive measures have not only reduced common drunkenness, but in an almost equal degree cut down the diseases and physical disability due to the use of alcohol, and have in this measure improved the public health.

C. V. C.

## REVIEWS

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NUTRITION AND CLINICAL DIETETICS. By HERBERT S. CARTER, A.M., M.D., PAUL E. HOWE, M.A., Ph.D., and HOWARD H. MASON, A.B., M.D. Philadelphia and New York: Lea & Febger, 1917.

THE recent rapid advances in our knowledge of physiological chemistry and nutritive processes in health and in disease have been so numerous and important that it was desirable that there should be a representative presentation of the subject in a carefully prepared text-book. It is just as true that the dietetic treatment of disease has undergone a radical readjustment, and there was need of a work that would give the outlines of modern scientific dietetics in a way available to the medical student and practitioner. The present volume is a splendid response to this demand.

The authors evidence a familiarity with the subject that is convincing, and they make a most interesting story. They show no bias, but when the views upon a topic under discussion have excited opposite opinions by men of standing, they present, as it were, "the evidence in the case" and let the reader reach a conclusion. They do not deny us their personal opinion or experience in these instances. A case in point is the article upon auto-intoxication. There are many other similar instances. The section devoted to the dietetic treatment of disease is written in a very readable way, sometimes suggesting a clinical discourse.

The work is not a practice of medicine with a lot of physiological and dietary heirlooms scattered here and there. It is a pleasure to lose Alexis St. Martin of the vintage of 1825. It is not even a poor cook-book with a medical flavor. If any criticism or suggestion were made it would be that more instruction on the preparation of food could have been combined with the other valuable divisions with advantage. It is generally conceded that the preparation of the food for the sick is as important as the selection of it.

The authors show much ability in collecting and presenting what is well established. They point out many popular fallacies and give convincing reasons for the statements made. What is known of vitamins and accessory foods is clearly told.

Part I is devoted to foods and normal nutrition, including the physiology of digestion, absorption, excretion, energy requirements,

and food economics. This last topic is particularly timely, and will prove helpful in formulating advice now in much demand. In the discussion of metabolic processes the new terminology has not been allowed to becloud the clear presentation of the subject.

Part II takes up the consideration of the various food elements. There is a refreshing change in the manner in which the subject is handled, and many stock statements are profitably omitted. There is a completeness and yet a conciseness that makes this section valuable.

Part III considers feeding in infancy and childhood and furnishes a good working guide. It is safe and sufficiently detailed to enable the practitioner to work out these troublesome cases. Many points made suggest a practical familiarity with the subject.

Part IV comprises half of the book. It is here that we note the scientific application of food adjustment to diseased conditions. There is pointed out what is required by the normally functioning organism, how the need is modified by the disease and how we may hope to administer the food suited to the changed condition. The article upon diet in circulatory diseases is very timely, and while helpful it points out the limitations imposed. Diet in aneurysm and "the senile heart" receive deservedly scant consideration.

It seems difficult to write diets without slipping into the old kind of directions. Just why layer cake is worse than other kinds for a case of asthma is not made clear. Again, beef-juice is said to "have considerable nutritive value." This preparation is troublesome to make, is expensive, and yields only 25 calories in 100 grams. It requires a half-pound of meat to yield this amount of juice. It might be remarked in passing that the white of an egg, poor as it is, will give more calories.

In the chapter on diseases of the stomach a good case has been made for a poor client in the article on indigestion. We may not agree as to existence of such a disease, but the article is worth reading.

The article on diabetes is of special interest at this time, and the chapter is very satisfactory. The Allen treatment is given in sufficient detail to enable one to understandingly apply it. The other methods of dieting in this disease are given due consideration. The writer does well to emphasize that the same thought and detailed care in ordering food for a patient that is given in the ordering of drugs will make a favorable change in our therapeutics.

Typhoid fever is another disease that has received an unusual measure of careful study from the angle of dietetics. The article upon the subject will be appreciated by all, whether they are champions of the high or low caloric feeding of these cases.

The article on feeding in arthritis deformans gives a satisfactory presentation of the evidence, and invites you to decide.

The book contains valuable tables of food values of practically all foods, according to the calorie worth of a given weight or the weight of a food required to yield a certain number of calories.

B. F. S.

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THE DIAGNOSTICS AND TREATMENT OF TROPICAL DISEASES. By E. R. STITT, Medical Director, United States Navy; Commanding Officer and Head of Department of Tropical Medicine, U. S. Naval Medical School. Second edition. Pp. 534; 117 illustrations. Philadelphia: P. Blakiston's Son & Co., 1917.

THE purpose of Dr. Stitt and the publishers in the original edition, and also in this second edition of the book in hand, has been to provide in compact pocket manual form a reasonably full clinical and laboratory guide in the field of tropical medicine. By special typography the use of a good thin paper and by the condensed form of presentation of facts in the text this in a large measure has been accomplished. The writer has had many occasions for consulting the older edition, and can testify to the usefulness and reliability of the work. The same plan and general scope apply to the second edition, which, however, has been increased in size by over 100 pages. These additions include the rewriting of numerous paragraphs throughout the volume and the insertion of new paragraphs to conform to and to introduce the advances in our knowledge of various affections, and also two new chapters.

One of these added chapters deals with special problems in diagnosis in the tropics and the peculiarities assumed by cosmopolitan diseases when occurring in tropical regions; the second with the clinical significance of special cutaneous manifestations and symptoms from the special sense organs in tropical diseases. The writer realizes the limitations of scope and size of the volume involved, and with such limitation accepted feels that much praise is to be accorded the book; yet he cannot but feel that a more extended discussion of animal parasitology and of animate disease carriers ought to be included. Dr. Stitt, for example, has no description of any species of tape-worm in the book, and has selected only those which manifest a more or less restrictedly tropical distribution for all of the helminths as proper for discussion. The writer feels this is a shortcoming which ought to be rectified. Some space for such material might be gained by foregoing special paragraphs upon "symptoms in detail," then frequently containing extensive repetitions of material already included in the general symptomatology of the various affections. If it be objected that such subjects are treated by the author in a separate volume, as is the case, it is to the writer's mind rather an argument for entire

reference of such affections to the other work or else to the combination of the two in future editions. In fact this last to the writer's way of thinking is eventually to be desired, and should easily be accomplished with a saving of from one-quarter to one-third of the combined pages of the two as they now exist.

A. J. S.

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**ROENTGEN TECHNIC (DIAGNOSTIC).** By NORMAN C. PRINCE, M.D., Attending Roentgenologist, Omaha Free Dental Dispensary for Children; Associate Roentgenologist, Douglas County Hospital, Bishop Clarkson Memorial Hospital, etc., Omaha. Pp. 140; 71 illustrations. St. Louis: C. V. Mosby Company, 1917.

THE author states as his object in presenting this book the instruction in roentgen technic of the general practitioner who is obliged to employ roentgen apparatus in addition to his other numerous duties. That such a book is very much needed is beyond question, but it is doubtful that this one can be recommended highly to serve this purpose. Naturally, it contains some good advice and some valuable information, but the subject has not received the careful attention that should be given to a work of instruction. The author deplors the fact that the untrained general practitioner does not know "the why and the wherefore of any process," and yet he fails decidedly in this very aspect of the subject. Certainly, the untutored mind would not grasp the principles of the fluoroscope, could not comprehend the identity of roentgen rays, nor feel certain of being able to control the output of a transformer to best advantage by a perusal of the pages. The space devoted to the details of case histories, records, and filing methods could have been better devoted to these other matters. One cannot overlook the thoughtlessness of practically advocating the use of bismuth subnitrate in gastro-intestinal examinations instead of warning against the dangers attending its employment. The best features of the book are some excellent illustrations showing the tube positions for examining many portions of the body.

H. K. P.

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**SURGICAL CLINICS OF CHICAGO.** A COMPILATION BY CHICAGO SURGEONS. Vol. I, No. 3. Pp. 230; 70 illustrations. Philadelphia and London: W. B. Saunders Company, 1917.

THIS number of the *Surgical Clinics* is the best one up to date. It contains 21 original articles written by some of its ablest men in Chicago. It is well and abundantly illustrated in a manner that

gives the greatest aid to the reader of the articles. Most of the articles are exceedingly well written and handle their subject in a complete and satisfying manner. The subjects too are very interesting ones and present richer infrequent, though exceedingly important, conditions that we can learn about only from such works as are here compiled. Text-books give us the classic presentations, but the work under discussion brings out these "sign-post" points that are so much appreciated by the clinician and surgeon. E. L. E.

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SEX HYGIENE. By FREDERIC HENRY GERRISH, M.D., LL.D.,  
Professor Emeritus of Surgery in Bowdoin College. Pp. 51.  
Boston: Gorhauss Press, 1917.

THIS little book really is the bound lecture given by the author to the Freshman Class in more than one college in the country. It is written for the young men and boys and is not technical in any sense of the word. The writer tells in a straightforward manner the plain every-day unvarnished truth about sex relation. He shows most clearly the dangers to health and happiness that may result from the violation of our sexual morals. It is a book that every young man should read. E. L. E.

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EXPERIMENTAL PHARMACOLOGY. By DENNIS E. JACKSON, Ph.D.,  
M.D., Associate Professor of Pharmacology, Washington Uni-  
versity Medical School, St. Louis. Pp. 536; 390 original illus-  
trations, including 24 full-page color plates. St. Louis: C. V.  
Mosby Company, 1917.

THE author has succeeded admirably in making the book what he intended it to be, namely, a laboratory manual. Not only is it useful for pharmacology students, but also for students of physiology. Each experiment is described in detail, and the accompanying illustrations are worthy of particular mention for their uniform excellence. As the author states, the purpose of the book is to develop experimentally a knowledge of the general principles of pharmacological reactions rather than to lay emphasis on a vast array of details regarding the specific action of a long list of substances.

Additional features are the chapters on shop work and photography and a list of dealers in apparatus, tools, supplies, equipment, etc. The book, as a whole, should find great favor both with instructors and students. H. C. D.

THE BIOLOGY OF TWINS. By HORATIO HACKETT NEWMAN, Professor of Zoölogy, University of Chicago. Pp. 185; 55 illustrations. Chicago: University of Chicago Press, 1917.

IN this neat volume are brought together, by a trained student of embryology, the facts about mammalian twins, followed by a discussion of the bearings of these facts on such fundamental problems as heredity, symmetry in development, and the factors controlling the sex of the offspring. The author's preparation for this work lies in his extended study of the embryology of the Texas nine-banded armadillo. This form exhibits one of the most remarkable examples of constant twinning in mammals. In a very early developmental stage the cells derived from the single fertilized ovum arrange themselves in four parts and each part develops into a separate individual. These four individuals coming from one egg cell are of very similar appearance and always of the same sex. In man, twins are of two kinds only: those derived from a single ovum, as in the armadillo, these being "identical twins," and those where each of the offspring comes from a separate fertilized ovum, where the individuals may be of different sex and of very dissimilar appearance. These and similar topics are treated of from the embryological stand-point. The author has assembled much interesting information, and while some parts of the work would be of greatest interest to special students of embryology and genetics, there is much of interest to the less specialized reader.

W. H. F. A.

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FOOD AND THE PRINCIPLES OF DIETETICS. By ROBERT HUTCHINSON, M.D., F.R.C.P., of London and Great Ormond Street Hospitals. Fourth edition. Pp. 580. New York: Wm. Wood & Co.

IN this fourth edition much has been rewritten, recent food analyses and tables added, diets reconstructed, and a chapter on vitamins added.

It is a complete detailed work on food—its analyses, preparations, uses, and values both in health and in disease. It is the essential building stones or basic principles with which he deals, and a thorough understanding of which is absolutely necessary to both physician and dietitian.

The last chapters, treating of food in disease, including valuable menus, are most interesting and useful.

It is for practitioners and students of medicine and for nurses and dietitians.

J. D.

# PROGRESS OF MEDICAL SCIENCE

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## SURGERY

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UNDER THE CHARGE OF

T. TURNER THOMAS, M.D.,

ASSOCIATE PROFESSOR OF APPLIED ANATOMY AND ASSOCIATE IN SURGERY IN THE  
UNIVERSITY OF PENNSYLVANIA; SURGEON TO THE PHILADELPHIA GENERAL  
HOSPITAL AND ASSISTANT SURGEON TO THE UNIVERSITY HOSPITAL.

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**Antiseptic Properties of Acriflavine and Proflavine, and Brilliant Green.**—BROWNING and THORNTON (*Brit. Med. Jour.*, 1917, xi, 70) says that flavine compounds and brilliant green are antiseptics which exert a slowly progressive bacterial action. Concentrations of these substances, which at first inhibit and finally kill bacteria, are without harmful effect on phagocytosis or on the tissues locally or generally; hence they are specially suited for therapeutic purposes in infected wounds. Flavine compounds may be applied to the peritoneum with safety. Flavine (acriflavine and proflavine) are enhanced in their bactericidal potency by the presence of serum; brilliant green, in common with most other antiseptics, is reduced in its activity by serum. The most suitable method of application of an antiseptic for therapeutic purposes must depend very greatly on its behavior in the presence of serum. When the serum is inactivated by serum, frequent renewal of the watery solution is indicated as in Carrel's procedure; this, of course, is only permissible provided that the substance is not in itself toxic. Brilliant green satisfies the requirements for application by repeated irrigation, as a powerful bactericidal solution (1:2000) is innocuous to the tissues. On the other hand, since flavine compounds are most bactericidal in serum, the indication is to arrange the wound dressing so that these antiseptics may act in a serum medium; also, since these bodies are not rapidly thrown out of action by serum, accumulative deposit should be prevented by avoiding too frequent additions of considerable quantities of the antiseptic solution. Clinical experiences have substantiated these conclusions, and the evidence at disposal points to the application of flavine bodies, by means of gauze packing or some appropriate modification of this procedure, as likely to yield the best results. Thus there is evidence that by taking full advantage of the properties of flavine bodies a relatively simple technic may be followed. The application of the flavine compounds,



especially for the purpose of preventing the onset of septic manifestations in early wounds, is emphasized; also their use for preventive exacerbations after operating on areas already infected. Operative measures are an essential preliminary to the effective use of therapeutic antiseptics in wounds, since the antiseptic can act only when brought into intimate contact with the infected tissues.

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**Localization of the Growing Point in the Epiphyseal Cartilage Plate of Bones.**—HAAS (*Am. Jour. Orthop. Surg.*, 1917, xv, 563) says that while it is an accepted fact that longitudinal growth of bone takes place in the region of the epiphyseal cartilage plate and that growth continues until that particular highly differentiated zone of cartilage undergoes complete ossification, the question arises as to the particular part which is most important in the production of the length growth. Haas carried out an experimental study on dogs in an effort to answer this question. He concluded that an incision through a growing bone at the junction of the metaphysis with the epiphysis always causes a disturbance in growth. A separation in the natural line of cleavage between the epiphysis and metaphysis, after incising the periosteum, causes some loss in length growth. It is possible in exceptional cases, in which a very minimal amount of injury is produced, that there will be no hindrance to growth. The excision of the metaphysis causes a very slight disturbance in growth. The excision of the epiphyseal cartilage plate causes practically a complete cessation of active longitudinal growth. The most active and important elements necessary for longitudinal growth are located in the columns of cartilage of the epiphyseal cartilage plate. A limited property of producing length growth is possessed by the cartilage adjacent to the columns of cartilage. The localization of the growing point of bone is of value in explaining the results of injury and disease to this particular region.

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**Bone and Joint Infections Treated by the Carrel Technic.**—HAWLEY (*Am. Jour. Orthop. Surg.*, 1917, xv, 586) believes that it requires at least one month of actual training to become familiar with the technic and that it is perfectly hopeless to expect to learn the method by reading the most complete description. He gives his reasons for his belief at length. The technic is reviewed as follows: Complete exposure of the infected tissues can never be too liberal or extensive. Pockets spell failure. Contact of the sterilizing agent should extend to every part of the wound surface. The object is progressive sterilization. This requires at each dressing as finished surgical asepsis as an abdominal operation. Gloves should be worn and instruments used instead of fingers. Two sets of instruments are preferred, one for the skin and one for the wound. The first step of the dressing is the mechanical sterilization of the skin. The vaselin is first removed by ether and then the skin cleansed very carefully with neutral sodium oleate. The second step is the mechanical sterilization of the wound by thorough scrubbing with sponges wet in oleate. This prepares the surface for the contact of the solution. It must be done thoroughly, but without trauma. The third step is the protection of the skin by anointing with sterile yellow vaselin, because Dakin's solution burns the skin. The fourth step is the placing of Carrel's tubes (with multiple fine holes and blind at

one end) throughout the wound. Gauze wet with the solution is placed around the tubes loosely. The solution is instilled every two hours sufficiently to fill the wound cavity. This has proved more satisfactory than the continuous drip. Reinfection is the defeat of this sterilizing process. This may be due to error of aseptic technic, defective mechanical sterilization of the skin or wound, defective solution, or failure to include every part of the wound. When the technic is incomplete the cases do well for a time and then remain stationary. When the technic is efficient and a case fails to progress it is a sure sign that a pocket exists. These are often impossible to locate unless the patient is given a general anesthetic. Reoperation is indicated when a case becomes stationary and whenever exposed bone persists. It is surprising how constant and how extensive these pockets are in non-progressive cases. Exposed bone always means necrosis, and the peculiar form of surface sequestration requires artificial separation. Spontaneous separation is unusually slow, but these surface moulds are easily loosened by gently tapping with a chisel. They usually lift off *en bloc*.

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**Results following the Treatment of Pelvic Inflammatory Lesions by Surgical Measures.**—CLARK and NORRIS (*Surg., Gynec. and Obst.*, xxv, 1917, 33) say that from a study of more than 500 cases in which the postoperative and remote results of surgical intervention in pyogenic infections in the Fallopian tubes were considered, they conclude that course of conservative treatment decreases mortality, and enhances the chances for securing a good functional restoration of the pelvic organs. In all cases of acute infections of the Fallopian tubes the patient should be kept under observation until the course of the case is defined. In the great majority the temperature subsides, the pain disappears, the tubal enlargements decrease to palpable proportions, and if the attack is a primary one the patient may be given a respite from operation until a recurrent attack supervenes. Even under these recurrent conditions the conservative policy is again pursued until subsidence takes place a second time, when an abdominal operation is advised, with a view to treating existing conditions to the best possible advantage. Usually both tubes are removed and the ovaries are conserved. If, under the conservative plan, the symptoms do not abate and the tube continues to enlarge, vaginal drainage is instituted, either by direct incision into the cul-de-sac or through the guidance of an abdominal incision. In the purulent lesions of the tubes all operative procedures are attended by a higher mortality and a greater morbidity, whereas under a conservative waiting treatment a patient will seldom die during an acute infection. In their series there was no death. In all hazardous cases the increasing severity of the symptoms and the enlargement of pelvic masses give ample warning and permit of a simple drainage operation that will tide the patient over the danger. When the acute attack has subsided the surgeon has the best opportunity for ascertaining, during the course of an operation, the exact degree of involvement of the tissues, and thus he is enabled to select the type of operation best suited to the individual case. Conservative operative procedures instituted with a view to restoring a closed Fallopian tube seldom restore fecundity. Plastic operations upon the fimbriated extremities of the Fallopian tubes, with a view of effecting restoration

of fecundity, are almost invariably failures and necessitate additional operations. They believe, therefore, that the safer policy is to remove the tubes by a wedge-shaped cornual resection in all doubtful cases, thus disregarding any attempt at restoration of fecundity. Hysterosalpingo-oöphorectomy in the sexually mature women, the subjects of chronic infections of the uterus and adnexa, is followed by a lower mortality and a greater certainty of restoration to health than are possible after conservative operations. Conservative operations employed with a view to preserving ovarian tissue should be limited chiefly to women under thirty years of age. The routine drainage of pus tubes through an abdominal incision is an unsatisfactory procedure from every standpoint and should not be resorted to if it can possibly be avoided.

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## THERAPEUTICS

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UNDER THE CHARGE OF

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**Clinical Observations on the Effect of Digitalis in Heart Disease with Pulsus Alternans.**—WINDLE (*Quart. Jour. Med.*; 1917, x, 275) points out that pulsus alternans must not be confounded with other types of pulse irregularity associated with alternating weak and strong pulse waves. A pulse tracing of pulsus alternans is characterized by the sequence of a strong and weak pulse which follow one another at equal time intervals, or the weaker pulse may occur a trifle ( $\frac{1}{10}$  of a second) late. The weaker contraction of the pulsus alternans never occurs prematurely under any circumstances, and the pause after it may be slightly shortened but is never prolonged. The cause of the pulsus alternans is an overtaxed heart. It can be produced experimentally by any procedure that leads to exhaustion of the heart, and it signifies a disproportion between the contractile power of the heart and the rate at which it is beating. From this the corollary necessarily follows that in pulsus alternans the slower the rate the greater the degree of exhaustion of the heart. Clinically pulsus alternans is met with in paroxysmal tachycardia, in acute toxic diseases, in severe cardiac failure from rheumatic lesions, and is most frequently associated with advanced and widespread arterial disease in the aged. This combination of pulsus alternans and advanced arterial disease is a certain forerunner of severe heart failure which will prove fatal within two or possibly three years. The prognostic importance of the type of pulse irregularity is very great, as it is the only form of pulse rhythm which in itself gives definite information about the functional efficiency of the heart. Windle's observations do not support the prevalent opinion that digitalis readily produces pulsus alternans or that in cases in which this type of pulse is present it aggravates the irregularity. In fact, Windle finds that digitalis frequently has the opposite effect;

that is, the pulses become more equal in force and the disparity in strength is temporarily abolished. The patient's symptoms are improved in all respects; these beneficial results often ensue coincidentally with a considerable rise in blood-pressure. Of the factors which influence the persistence, increase, decrease, or abolition of alternation, the rate of the heart is most potent. As a rule it is customary to find alternation increased with an increase and decreased with a slowing of the pulse-rate. In some patients there appears to be a critical rate, above which alternation develops and below which alternation is absent. Pulsus alternans appeared after digitalis in only one healthy heart and in only one patient suffering from cardiac disease. Many cardiac patients show, under full doses of digitalis, a pulse resembling pulsus alternans, but measurements indicate that premature contractions account for the weak beats. Windle has noted the effects of digitalis on the pulse in over a hundred cases of heart disease with pulsus alternans. The drug has been given in varying doses and for weeks at a time, but he has never found an increase in alternation of the pulse which could be ascribed to the drug or harm result to the patient. The beneficial effects of digitalis in heart disease with pulsus alternans are largely due to its action in restoring the tonicity of the heart and slowing its rate. The relation between heart-rate and pulsus alternans is emphasized by the fact that Windle never found alternation disappear in the absence of cardiac slowing. The rate of pulse at which alternation ceases varies widely, but it is unusual for alternation to persist when the pulse falls to about the normal rate. When alternation does persist prognosis is bad.

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**Effect of Undernutrition on Muscular Force.**—WILLIAMS (*Arch. Int. Med.*, 1917, xx, 399) has determined the effect of the prolonged use of the Allen treatment on the physical vigor of diabetic patients. As is well known the Allen treatment consists essentially in such dietetic measures as will keep the patient acid- and sugar-free. This usually calls for a diet far below the caloric value necessary to maintain a normal individual in good health. From a large series of dynamometer tests Williams concludes that diabetics, as a rule, are distinctly weaker than normal persons. This weakness may be due in part to loss of bodily musculature, but it is probable that the lessened amount of food metabolized by diabetics does not provide sufficient energy for their normal exercise requirements. There appears to be a direct relationship between food tolerance and muscular vigor, for as food tolerance increases so does muscular vigor, and a decline in food tolerance is accompanied by a loss of physical strength. Williams finds that diabetics kept on a low calory diet for months continue to gain in physical vigor provided the diet is just within their maximal metabolic capacity. This is in accord with the clinical experience that nutrition within the tolerance of the patient gives the greatest comfort, strength, and sense of well-being. Another very interesting point brought out by Williams is that while diabetics living on a diet below normal physiological requirements possess a diminished muscular tone, feeding them beyond their metabolic limitations causes not only a further reduction in their food-tolerance but also an even greater loss of strength. Williams can find no justification for the common notion that overfeeding causes

even a temporary increase in comfort or bodily strength. It appears from this investigation that diabetics gain in physical vigor as they become and remain sugar-free, while overfeeding causes a definite and often a serious loss of strength.

**Influence of Large Doses of Digitalis and Digitoxin on the Blood-pressures of Man.**—EGGLESTON (*Jour. Am. Med. Assn.*, 1917, lxi, 951) reviews briefly the literature, pointing out the fallacy of arguing the analogy between the toxic action of digitalis bodies on animals and the therapeutic action on man. From his study of fourteen carefully controlled hospital patients, receiving standardized digitalis and digitoxin, Eggleston concludes that digitalis and digitoxin have very little influence on the systolic pressure in either direction; that these drugs tend to produce a significant reduction in the diastolic pressure; and that they tend to produce a material increase in pulse-pressure. An analysis of the relation between the cardiac slowing and the fall in diastolic pressure failed to show that the alteration in the pulse-rate accounted for the changes occurring in the diastolic pressure. Nor was there any relationship between the changes in pulse-rate and those in the systolic pressure. Eggleston believes that neither digitalis nor digitoxin has any direct action on the vessels when given to man even in large therapeutic doses. Admitting that the digitalis bodies are capable of increasing the systolic volume output of the heart, Eggleston explains the changes in systolic, diastolic, and pulse-pressures resulting from the administration of these drugs as follows: Digitalis, by improving the circulation, leads to improved pulmonary circulation with the relief of cyanosis and the abolition of the stimulating effect of carbon dioxide on the vasomotor center. The improved circulation results in the more normal functioning of the various organs and tissues, and tends to restore to normal the several mechanisms by which the circulation is maintained at the most efficient level. On this hypothesis one may expect to find that the net changes in the systolic, diastolic, and pulse-pressures would differ in different cases in order best to meet the conditions prevailing. This is precisely what Eggleston has found to occur in his cases and it also explains the apparently divergent results of different observers. The observation that the pulse-pressure is increased in the majority of cases showing material clinical improvement as a result of digitalis is also in harmony with this hypothesis, since the pulse-pressure is to a certain extent a measure of the efficiency of the circulation through the periphery.

**Clinical Studies of the Respiration. III. A Mechanical Factor in the Production of Dyspnea in Patients with Cardiac Disease.**—PEABODY reports (*Arch. Int. Med.*, 1917, xx, 433) the effect on the respiration of normal persons and cardiac patients when there is a progressive rise in the carbon dioxide and a progressive decrease in the oxygen of the air breathed. The subjects of the experiment breathed into and out of a closed system until dyspnea became so distressing that the experiment had to be discontinued. Comparing the effects on normal subjects and on cardiac patients, Peabody found that in both classes of persons the rate of breathing was doubled; the depth of breathing was increased fourfold in normal but only twofold in cardiac cases; the

minute volume rose by 700 per cent. in healthy persons but only by 170 per cent. in cardiac patients; the carbon dioxide in the inspired air at the end of the experiment was between 7.11 and 9.22 per cent. for the normals and between 4.27 and 5.62 per cent. for the cardiacs. The cardiac patients became dyspneic when the carbon dioxide in the inspired air was but little more than half that required to produce dyspnea in normal subjects. This does not mean that cardiac patients are more susceptible to carbon dioxide. It means that cardiac patients become dyspneic more easily than healthy subjects because of their inability to increase the depth of breathing in a normal manner and thus prevent the accumulation of carbon dioxide in the blood and tissues.

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## PEDIATRICS

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UNDER THE CHARGE OF

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**Comparison between Clinical Examination and Roentgenograms in Diseases of the Chest.**—CHAPIN (*Am. Jour. Obst. and Dis. of Women and Children*, October, 1917, vol. lxxvi, No. 478). Owing to the difficulty of keeping little children quiet during exposure it is often hard to interpret heart shadows. A twisting of the body may cause a rotation of the chest so as to exaggerate the heart shadow in any direction. Of 15 cases studied both by *x*-rays and by physical examination, 7 showed an agreement, or partly agreed, and 7 failed to show a correspondence in the conclusions reached by the two methods. In regard to the lungs a combined study was made in 97 cases. There was agreement in 77 and disagreement in 20 cases. Of the latter 5 gave evidence of lobar pneumonia that was not detected by physical examination; 2 gave physical signs of pneumonia, which were not confirmed by *x*-rays; 3 showed physical signs of bronchopneumonia not found in *x*-rays. As a general rule it was found that the *x*-rays would often give a shadow in the absence of physical signs in congestion, small consolidations, hilum infiltrations, interlobar pleurisy, miliary tuberculosis, and mediastinal tumors.

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**Hunger in the Infant.**—TAYLOR (*Am. Jour. Dis. of Children*, October, 1917, vol. xiv, No. 4) quotes previous writers confirming the fact that hunger contractions are greater in the newborn infant, and states that still greater hunger contractions are present in the prematurely born infants. No relation exists between cyanosis and hunger contractions. In young infants the taking of food into the mouth does not inhibit hunger contractions, but this does occur in older children. This is psychic in character. Even in younger infants the presence of food in the stomach causes reflex inhibition, although in the younger infants it may be only partly developed. During the hunger state

successive automatic sucking movements (each sucking act being the stimulus for its successor) are present. In normally developing breast-fed infants hunger is not ordinarily an immediate cause of crying. In premature infants under one month the average time required for the development of hunger is one hour and forty minutes, with a maximum of two hours and twenty minutes and a minimum of forty minutes. In full-term infants under two weeks the average time is two hours and fifty minutes with a maximum of four hours and a minimum of two hours. In infants from two weeks to four months the average time is three hours and forty minutes with a maximum of four hours and thirty-five minutes and a minimum of three hours and twelve minutes. This time for the development of hunger in any one infant is fairly constant. In chronic nourishment disturbance the interval is shorter, as it is also when food is poorly tolerated. The hunger contractions occur long before the stomach is empty, so that is not necessarily an indication for more food. Feeble nursing power is not due to derangement of hunger apparatus. In pyloric stenosis hunger contractions are increased.

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**Appendicitis in Infants.**—ABT (*Arch. Pediat.*, September, 1917, vol. xxxiv, No. 9). The diagnosis is very difficult as the symptoms vary greatly from those in older children and adults. The almost complete absence of subjective symptoms in infants makes the diagnosis almost impossible. Pain and tenderness are difficult to elicit and more difficult to localize. Vomiting occurs so frequently in the gastro-intestinal, nutritional and toxic diseases of infants that it is of little value. Muscle spasm or rigidity of the right rectus may be present early, but it is difficult to elicit. Manifest chill, which is rare in childhood, is sometimes noticed early. Temperature is unreliable. The pulse usually follows the temperature. Rupture of the appendix may give temporary amelioration of the symptoms. Constipation is the rule and occurs among the more severe types. Diarrhea is present in the milder types. Traumatism may be a factor in the etiology. There is a hereditary predisposition occurring in certain families. Foreign bodies such as concretions or worms may be the cause. Blood examination reveals a polymorphonuclear leukocytosis. In infants the diagnosis is extremely difficult and the mortality is very high. Rectal examination is of great value.

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**Empyema; Simple, Interrupted, and Continuous Aspiration.**—RICHTER (*Arch. Pediat.*, September, 1917, vol. xxxiv, No. 9). The mortality in this condition is very high. Holt reported a loss of 50 per cent. in a series of 150 cases. Seventy-five per cent. of those in the first year of life were lost. The deaths are due to (1) loss of proteid material from prolonged suppuration. (2) Intoxication of suppuration. (3) Collapse of the infants' lungs, the median diaphragm being so frail that the opposite lung loses much of its volume. The intoxication of suppuration may be controlled by drainage. Incision or drainage does good temporarily, but the child gradually fails and dies during the second, third, or fourth week. This is due to infection plus the loss of large quantities of fluids and proteids. The third factor above may develop acutely immediately after any drainage operation. Pus in pleura differs from abscess elsewhere. It becomes sterile if not con-

taminated from outside. Aspiration is the simplest form of treatment if done in a rational manner. The pus should be aspirated in small quantities, and it is not absolutely necessary to remove all, even in this way, as a small collection of sterile fluid will be absorbed. By removing a small quantity the temperature, respiration, and pulse are favorably influenced. As aspirations proceed the pus becomes thicker. This signifies less acute infection and absorption of the serous element. This is distinctly poorer in bacteria. The author uses an exploratory needle of moderate size and about four feet of rubber tubing. This is filled with sterile water and the needle is inserted in the sixth or seventh interspace; the other end of the tube is allowed to hang in a receptacle containing water. As soon as pus begins to flow the vessel containing the end of the tube should be elevated until the column of water in the tube is not more than two or three feet in height. When infection is not controlled and an increasing degree of intoxication demands different treatment, continuous aspiration is used and usually produces a better result.

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**Pneumonia in Early Infancy and Childhood; its Mortality and Treatment, with Special Reference to the Use of Alcohol.**—KOPLIK (*Jour. Am. Med. Assn.*, November 17, 1917, lxi, No. 20) writes of a study of 1351 cases from 1906 to 1914 and of 391 cases from 1914 to 1917. The first group consists of cases that were treated with alcohol either entirely or in some cases. The second group consists of cases in which no alcohol was used. The tables show that the younger the infant the worse the prognosis. The greater mortality occurred below the age of one year and that the mortality decreased steadily after the fourth year. All of the cases below the age of one year were of the bronchopneumonic type. Of 248 deaths below the age of ten years, 192 died of or with complications. From the second year up the incidence of complications diminished markedly. The principal complications involved the gastro-intestinal tract. Congenital heart lesions, measles, diphtheria, pertussis, nephritis, sepsis, erysipelas, and tuberculosis of the abdomen were met with. Next to the gastro-intestinal complications the most serious was meningitis. It was invariably fatal when complicating the pneumonia during the first year. In infants there seem to be no difference whether the child was breast-fed or bottle-fed. The treatment recommended is, first, proper nursing and feeding, and second, to support the strength of the patient, being on the lookout for complications and meeting them as quickly as possible. In the first group of 1351 cases there were two distinct periods. The first period is during the years in which whisky was used freely and the second when alcohol was used less and less each year. The second main group comprises the cases in which no alcohol was used. The tables show a decided decrease of the mortality rate for all ages in the cases in which no alcohol was used. In short, the author recommends the expectant or symptomatic treatment of pneumonia, using caffeine, camphor, digitalis, and kindred drugs as the indications arise.



## OBSTETRICS

UNDER THE CHARGE OF

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**Labor Complicated by Complete Rupture of the Uterus at Full Term, without Hemorrhage or Shock, followed by Recovery.**—NEILL (*Am. Jour. Obst.*, February, 1917) reports the case of a young negress admitted to the Columbia Hospital, Washington, with a temperature of 102°, pulse 120. She had been in labor three days, but walked from the third floor of her home to the ambulance. On measuring her pelvis a considerably contracted but fairly uniform pelvis was found. The uterus extended to the seventh rib on the left side and fetal heart sounds were heard strongly in the left lower quadrant. The membranes had not ruptured. There was full dilatation and the vagina was very shallow. The patient was prepared for delivery. It was necessary to give three enemas before the bowels could be emptied. Later the membranes were artificially ruptured, followed by the escape of an ounce of fresh blood and very little amniotic liquid. The patient's pulse and temperature were normal. She complained of continuous pain. The uterus was contracted and extended high up in the epigastric region. She was examined later, when a large tumor was found filling the pelvis and pushed well down into the vagina. It was thought to be a fibroid or gumma and almost completely filled the vaginal cavity. The cervix was retracted. The patient was prepared for immediate operation and a median low incision was made and the abdomen opened at the umbilicus. The bladder had been drawn up and was accidentally opened for about one and one-half inches on the anterior wall. This was immediately repaired and the incision in the abdomen extended higher up. There was free yellow fluid, but no blood, in the abdominal cavity. The fundus of the uterus extended well up under the ribs. The hand was passed behind the uterus and the umbilical cord was brought up into the incision. The fundus was then torn out of the abdomen and the child appeared through the rent in the posterior, lower segment, three and one-half inches long, occurring at the contraction ring. The child and placenta were immediately removed; the uterus brought well up into the wound and the body of the uterus amputated after dissecting off the bladder. The cervix was closed as in an ordinary hysterectomy. No tumor could be seen in the pelvis, which was attached to the uterus, but there was a hard mass behind the rectum and peritoneum filling the pelvic cavity about two-thirds. The patient endured the operation well. The child weighed 5 pounds 14 ounces. The mother made a good recovery, but had a slightly elevated temperature. Some time after, under an anesthetic, a transverse incision was made in the posterior wall of the rectum behind the sphincter. The rectal wall dissected up and a finger introduced behind the bowel. A hard mass occupying about two-thirds of the pelvic cavity and without fluctuation was found. A piece of this tumor was excised

and the wound in the rectum closed. The patient had no trouble whatever after this operation, nor did it interfere with the bowel function. The tumor was found to be myofibroma undergoing myxomatous degeneration.

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**Case of Interstitial Pregnancy Complicated by Labor.**—STONE (*Am. Jour. Obst.*, February, 1917) reports the case of a multipara, five and one-half months pregnant, taken with symptoms of intravaginal pregnancy. There had been pain in the right side, and a diagnosis had been made of pregnancy in the right broad ligament, or that the uterus contained a fibroid in or near the broad ligament. On examination the os was soft, but there was no reason to suspect intra-uterine pregnancy. The abdomen was distended by the tumor, movable, but strongly inclined to the right side, not unlike a pregnant uterus. The fetal body could not be made out. After waiting thirty-six hours for the condition of the patient to improve the abdomen was opened, when free hemorrhage was found, proceeding from rupture of the upper part of the tumor. A large quantity of blood poured out of the incision. A rapid supravaginal hysterectomy was done, which showed the extent of the hemorrhage. When the specimen was examined the uterine wall was found very thin. Rupture had occurred because of the thinness of the wall from the intermittent contractions of pregnancy, although the patient was not in active, full-term labor.

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**Labor Complicated by Emphysema.**—MURRAY (*British Med. Jour.*, January 6, 1917) was called to a primipara who was attended by a midwife and had been in labor fourteen hours. She presented a most alarming appearance. The face was scarlet and swollen to twice its normal size, both eyes being completely closed. The upper part of the chest wall and neck were much swollen and the affected parts presented the appearance of subcutaneous emphysema, being soft to the touch and with fine crepitations. This was interfering with respiration, so that the patient seemed to be in a dying condition. It was thought best to immediately deliver by forceps and a very large child was born. Twenty-four hours after labor the emphysema had somewhat subsided. The condition had undoubtedly arisen from the efforts of the patient in straining, probably with the mouth closed. Similar cases on record show that this accident is preceded by strong contractions of the uterus supplemented by vigorous general exertions on the part of the mother. While the condition is alarming at first sight it is rarely attended by much danger to life.

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**Retraction of the Uterine Muscle in Obstructed Labor.**—NICKS (*British Med. Jour.*, October 14, 1916) describes the case of a primipara, aged thirty years, rather short in stature and with a large cranium, who was in labor at full term. When seen the fetal head was high above the brim and freely movable. The cervix hung loosely below the presenting part. Labor went on to full dilatation, but the presenting part did not descend. A few hours later the membranes ruptured, forceps were applied to the sides of the head, but moderate traction failed to bring the head down. A second application of forceps was made some time later without result. A third forceps application was subsequently

made. Forty hours after the onset of labor, the patient was examined, and was found to have a rachitic, flat and generally contracted pelvis of moderate degree of contraction. The fetal head seemed to be of normal size. On passing the hand above the head, a thick band of uterine muscle was found constricting the neck of the child. The uterus had become tonically contracted, with the head of the child high above the brim. As it was impossible to take the patient to the hospital, she was deeply anesthetized with chloroform and an effort made to bring down the head with a cephalotribe. The fetus and uterus had become, as it were, one welded mass. Although the whole could be brought down by traction, it immediately went back to its original position. Accordingly, Cesarean section was done, the patient dying soon afterward. In these cases, there is some form of contraction or distortion of the pelvic brim. The head does not engage, but remains high above the brim and very mobile. The uterus continues to contract and retract, the cervix hangs down unfilled by the presenting part. The uterine muscle becomes tetanic and grasps the neck of the fetus above the brim; the shoulders cannot pass nor can the fetal head rise. The uterine cavity becomes hour-glass in shape, the upper portion contains the trunk, and the lower the head. As retraction progresses, the uterus molds itself to the fetal trunk and neck, while the lower zone becomes progressively thinner. This condition may come a few hours after the rupture of the membranes, and, when once established, constitutes one of the most terrible complications met with in obstetric surgery. Attention is drawn by the writer to the fact that a high and mobile fetal head occurring in a primiparous woman means trouble. If the practitioner thinks there is room enough to allow forceps delivery, and the fetal head is high above the brim and freely movable, the patient must be placed deeply under chloroform. If moderate traction fails to bring the head into the uterus, no further attempts should be made. The writer concludes that one must be especially careful when dealing with a short, thick-set woman who has a square head and short long-bones. A high position of the fetal head occurring in a primipara denotes serious trouble. While measurement of the diameter of the pelvis is useful, it is not conclusive, as the brim may be obliquely distorted and this will prevent the head from entering the brim, and at the same time will correspond with the indications given by measurement. The application of forceps to a fetal head which is movable and high above the brim is an obstetric operation requiring the most careful consideration. If the examining hand can be passed easily beyond the shoulders of the fetus, an attempt at delivery with instruments may be made. If there is the least evidence that the uterine muscle is retracted and around the neck of the fetus, Cesarean section should at once be performed. When the retraction ring is formed around the neck of the fetus, it will grip it firmly until the patient is almost at the point of death. The extraordinary example of bad obstetric practice arose from the fact that physicians are still found who believe that it is justifiable to apply the obstetric forceps to the unengaged head, and that, by introducing the hand or fingers within the vagina, a physician can tell how large the fetal head is and can be sure that it will enter the pelvis. There is but one rule of safe obstetric practice and that is that the obstetric forceps should never be applied

to the head until the head has entered the pelvic brim thoroughly, and one-half or three-quarters of its bulk has descended into the cavity of the pelvis. If the head remains high above the pelvic brim after sufficient uterine contractions have occurred to cause it to enter, if the physician can be sure, through external and internal pelvimetry, that the pelvis is normal or greater than normal in size, and the size of the uterus indicates that the size of the child is not excessive in development, version may be performed, followed by cautious extraction. This will place the risk upon the child, with considerable risk to the mother. If possible, such a case should be immediately removed to the hospital and delivered by section. It will give the best chance to both mother and child. It seems almost incredible that in a civilized country a woman should be allowed to be in labor for two days with three applications of the forceps and with a contracted pelvis before the necessity for Cesarean section became apparent.

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## GYNÉCOLOGY

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**Endocrinology and Gynecology.**—At the last meeting of the American Gynecological Society a very interesting symposium was presented on the relation of the glands of internal secretion to gynecology and obstetrics (*Surg., Gyn. and Obst.*, 1917, xxv, 225 to 359). In the introduction to this symposium, Frank said that in every department of knowledge it is expedient at intervals to stop, examine, and meditate, to "take stock," so to speak, of closed, open and future prospects; therefore, it will be well worth while to present the main conclusions that were presented at this meeting. Goetsch stated that there is a close interrelationship in function between the pituitary and sex glands, a fact supported by abundant experimental evidence and by numerous observations on pituitary disturbances in the human subject. Overfunction of the anterior lobe of the pituitary body is associated with overactivity of the sex glands while deficiency of pituitary secretion in the individual is followed by underdevelopment and genital aplasia in the young and by sexual inactivity and retrogression in the adult. Primary alterations in the function of the sex glands, as in pregnancy and after castration, are followed by pituitary hypertrophy and hyperplasia. The specific action of the extract of the posterior lobe of the pituitary gland, commonly known as "pituitrin," upon the smooth musculature of the uterus and bowel has led to the wide usage of this drug in obstetrical practice and in the treatment of intestinal paresis following abdominal and pelvic operations, and lastly the administration of pituitary extracts is of distinct benefit in clinical states of pituitary underfunction. From the lack of unanimity in the literature,

any conclusions as to the details of pineal gland function must be made flexible rather than dogmatic. However, McCord believes that a clinical syndrome is to be associated with disturbances of the functions of the pineal gland. Because of the involution of the pineal gland at puberty, the constitutional manifestations of pineal gland pathology appear to be confined to prepuberty years. The essential characteristics (apart from pressure and neighborhood manifestations) are (a) early sexual development evidenced in the enlarged genitalia, pubic hair, general body hair, early change in voice; (b) precocious mental development, manifested in maturity of thought and speech; (c) general overgrowth of body to the extent that a child of six or seven years may have the appearance of a child near puberty. McCord states that the inference is allowable that the pineal gland is an organ of internal secretion whose functions, however, are of minor significance in the general activities of the endocrinous system. As a result of his investigations, Pool states that no direct relationship has been established between the parathyroids and the female sex organs; no morphological changes in the parathyroids have been noted during pregnancy, yet apparently there is a connection between the parathyroids and the sex processes in the female, since tetany, the clinical evidence of insufficient parathyroid function, is somewhat prone to occur in menstruating, pregnant and puerperal women, as well as patients suffering from gynecological diseases or who have undergone gynecological operations. The vigorous research that has been expended upon the thymus gland during the past few years has not, on the whole, been very fruitful according to Pappenheimer. That the thymus serves an important function, especially in the growing organism, cannot be doubted. The organ is conspicuously large, has a characteristic structure, which is maintained with but slight variation in all classes of vertebrates, reacts in a very definite way to a variety of injuries, and has a constant relation to the development of the sexual organs. There are, furthermore, obscure but undeniable correlations with thyroid, adrenal and possibly other organs of internal secretion. Although these general facts seem established, yet in every detail of structure and physiology there has been, and is, the greatest conflict as to facts and interpretations. The fundamental problems of thymus physiology remain unsolved, and the established facts, which concern chiefly the normal and abnormal structure of the gland, are not such as lend themselves to clinical application. Carlson presented a most exhaustive paper on the endocrine function of the pancreas, in which he concluded that there is at present no evidence of any specific relations of the endocrine functions of the pancreas to the gonads, male or female, or to menstruation, pregnancy and lactation. Absolute diabetes, induced after conception, leads to death of the fetus; furthermore, absolute diabetes probably renders conception impossible. Partial diabetes under careful dietary control permits of normal sex life of women, and pregnancy under such conditions does not aggravate the diabetes, but in the absence of such dietary control the condition of pregnancy aggravates the diabetes in the mother and uncontrolled diabetes in the mother is extremely injurious to the fetus. There is some evidence that in the late stages of pregnancy the fetal pancreas may functionate for the mother. In considering the internal secretion of the adrenal bodies, Vincent

recalled the fact that the adrenal body represents the anatomical association of two elements, each of which is derived from a separate and independent system. The adrenal proper, or "cortex," is part of the interrenal system, while the medulla is simply the accumulation of chromophil cells of the same nature histologically, chemically, and pharmacodynamically as similar masses of cells in other parts of the body and there is no clear evidence that these two systems are functionally related. The medulla is developed from the sympathetic nervous system and its duty seems to be to facilitate the functions of this system in certain physiological emergencies. The adrenal cortex is developed from the germ epithelium; and the evidence is now strongly in favor of the view that it has certain important functions in connection with the growth and development of the sex organs. There is a considerable amount of clinical evidence that tumors of the adrenal cortex are frequently associated with sex abnormalities, evidenced in the female by an accentuation of male secondary sexual characteristics and simultaneously a hypoplastic condition of the internal generative organs. That Halban was correct in ascribing to the placenta an action upon the uterus and breasts has been proved by the experimental work of the last decade, according to a statement made by Frank in his contribution to this symposium. Placental extracts (mainly the lipoid fraction) rapidly induce hyperplasia of the uterus and breast (gland tissue and nipples) in castrates or in non-castrated animals. The chemical substance which induces these changes is thermostable, very resistant to strong alkalis and acids, and completely soluble in 95 per cent. alcohol, and it appears identical in its physical, chemical, and biological properties with a similar substance obtained from the corpus luteum. This substance can exert its influence in the absence of the thyroids, adrenals, pancreas, or in the absence of the thyroid and adrenals combined. In view of the apparent identity of corpus luteum and placental substance the question arises whether the placenta acts merely as a storage reservoir for corpus luteum secretion during the latter half of pregnancy or whether the placenta elaborates a hormone of its own. A rather extensive and extremely interesting paper on the relation of the ovary to the uterus and mammary gland from the experimental aspect was presented by Loeb in which he stated that an elaborate self-regulating mechanism controls ovulation. While normally the corpus luteum inhibits ovulation to the extent of permitting one ovulation in a month, during pregnancy the life of the corpus luteum is prolonged. Experimentally, ovulation can be influenced at will, accelerated by excising all corpora lutea, or retarded by producing artificial deciduomata. This retarding action of the corpus luteum is chemical, not mechanical. The corpus luteum also has a sensitizing action upon the uterus. This action can be analyzed by experimental methods. If the uterus is incised or mechanically stimulated at the time during which the corpus luteum is elaborating this growth substance, maternal placenta is formed. The mechanical stimuli, therefore, assume in this respect the function which the ovum exerts under normal conditions. In addition to these functions of the corpus luteum the ovary has a trophic influence on the genitals and likewise controls the development of the mammary gland.

## PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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**Myeloma with Metastasis to Liver and Spleen.**—Text-books generally assert that in myeloma no metastases are found. The classification of this type of tumor is not easy, due, in part, to the variety of elements, lymphatic or myelogenous, from which its cells may be derived. To add to the confusion there is the theory of Lubarsch that there may be in some organs, as the liver, spleen, lymph glands, and other lymphatic tissues, outside of the medulla of bones, deposits of hemopoietic or myeloid cells, which, simultaneously with the beginning of tumor growth in bone marrow, may assume a similar vegetative function. PEPPER and PEARCE (*Jour. Med. Res.*, 1917, xxxvii, 171) present the case of a man, aged fifty-two years, who for four years before his death had suffered from bronchitis and severe shooting and aching pains in the back and legs. The blood picture showed: Hemoglobin, 58 per cent.; red corpuscles, 3,370,000; leukocytes, 5100; differential count: polymorphonuclear neutrophiles, 39 per cent.; small lymphocytes, 51 per cent.; large mononuclears, 3 per cent.; transitionals, 3.5 per cent.; eosinophiles, 1.5 per cent.; basophiles, 1 per cent. Normoblasts were present. Bence-Jones protein was excreted in the urine at a high level for at least eighteen months before death. Roentgen-ray pictures of the spine and long bones were normal. At autopsy, myeloma of pelvis, vertebrae, and ribs was evident. The cells were of the plasma type. In microscopic examination of sections, masses of very similar plasma cells were seen about the portal spaces. A similar finding was noted in the pulp of the spleen, and these were considered probable foci of myeloma cells. By the use of tests for oxidase no granules could be demonstrated in any of the tumor cells in bone marrow, liver, or spleen, thus strengthening the belief that they were plasma cells. The authors have collected 15 cases, showing possible metastases of myeloma, 6 of which, including metastasis to liver, ovaries, lymph nodes, and tonsils, they consider transfers by some process other than by direct extension. Under Sternberg's classification the condition would be named a plasma-cell myeloma.

**Acid-fast Organisms in Distilled Water.**—KEILTY (*Jour. Med. Res.*, 1917, xxxvii, 183) emphasizes the importance in bacteriological work of using sterile distilled water collected in sterile stills, tanks, and bottles,

i. e., freshly distilled water collected and kept under sterile precautions. From examinations of specimens of water from stills and supply bottles he concludes that "all distilled water unless distilled in a sterilized apparatus and collected in sterile bottles will show bacteria, and if collected and allowed to stand, acid-fast organisms may develop which, in some cases, are morphologically and tinctorially like the tubercle bacillus."

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**Complement-fixation in Tuberculosis.**—CORPER (*Jour. Infect. Dis.*, September, 1916, vol. xix, No. 3) reports that clinical findings in tuberculosis give information regarding activity or inactivity only in a vague way, and thus far biological methods of diagnosis have been of little practical value, with the exception of the complement-fixation test. The most reliable investigators concede that a suspension of living tubercle bacilli is the only antigen which is of specific value. The objections to this antigen led the author to attempt to obtain an antigen from the tubercle bacillus by processes as nearly identical with those that occur in the body as possible. An autolysate was made by suspending tubercle bacilli in sterile salt solution for from six to eight days, and by tests it was shown that such an autolysate grew stronger in antigen titer coincidentally with the occurrence of autolysis. A comparison was made in a large series of cases of the autolysate antigen with the bacillary emulsion and the former was found to possess the following advantages: (1) it has a much larger range between the antigenic and anticomplementary doses; (2) it does not lose its titer when kept on ice; (3) it produces no interfering turbidity in the hemolytic system; (4) it is more specific than the bacillary emulsion. The examination of 361 persons (25 normal, 11 questionably non-tuberculous and 325 definitely tuberculous), using both an emulsion and an autolysate prepared from living virulent human tubercle bacilli, shows that: (1) The complement-fixation test for tuberculosis is not absolute, being positive only in about 30 per cent. of all the clinically definite cases of tuberculosis both active and inactive. Active cases give a higher percentage of positive results than inactive cases. (2) The value of the complement-fixation test for tuberculosis lies in the fact that, taken in connection with other findings, a definitely positive reaction makes the diagnosis of tuberculosis certain. (3) The absence of a reaction in non-tuberculous cases makes the test when positive more valuable than any other biological test.

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**Pathology of Worm Infection of the Vermiform Appendix.**—In 1899 attention was first attracted to the presence of the oxyuris in the appendix, and although many authors have since then repeatedly reported the presence of different kinds of worms in the lumen of the appendix, no serious credence has been given the claim that this agent was of importance in appendicitis. The majority of the studies upon worm infection in the appendix have been made in France. MATSUOKA (*Jour. Path. and Bact.*, 1917, xxi, 221) undertook a minute study of the parasites and their relationship to the tissues of the appendix. The study included 103 appendices removed at operation and 23 specimens obtained at postmortem. Of the 103 operative appendices, 48 were demonstrated to contain either worms or their ova. This indicated



that in his material nearly every second person had parasites in the appendix. The parasites were present in a much higher percentage of women than men. The greatest frequency of infection occurred between the ages of eleven and thirty. The types of parasites varied, the oxyuris being most frequent. Inflammation was present only in a portion of the cases containing parasites, and in those instances where the reaction was present it appeared localized to the immediate vicinity of the worm. In the 23 specimens which were obtained at postmortem, 6 showed the presence of worms. He believes that the worms are not directly or indirectly the cause of appendicitis. He believes, however, that the presence of the worm within the appendix may give rise to symptoms simulating clinical appendicitis.

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## HYGIENE AND PUBLIC HEALTH

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**American Mortality Statistics and Mills.—Reinke Phenomenon.**—FINK (*Jour. Infect. Dis.*, July, 1917, p. 62) has tabulated the detailed mortality statistics of Chicago, Cincinnati, Columbus, Philadelphia, and Pittsburgh for a definite period before and after purification of their water supplies. Similar figures for New York City and Boston, Mass., covering the same years have served as controls. In addition to a comparison of the crude death-rates with the death-rates from typhoid fever, malarial fever and diarrhea and enteritis, the death-rates of those diseases known to be sequelæ of typhoid fever have been especially studied. Curves of the death-rates from pulmonary tuberculosis, pneumonia, nephritis and heart disease have also been plotted to see whether during the three years immediately following years of high typhoid mortality there could be demonstrated a sudden rise in mortality from these diseases, a possibility which the data published by Dublin would seem to suggest. No striking evidence has been found that the Mills-Reinke phenomenon and Hazen's theorem apply to these cities when compared with control cities. The figures indicate a great variation among the cities studied including the controls. There is, therefore, a lack of uniformity in the appearance of the Mills-Reinke phenomenon and Hazen's theorem, since some of the cities thus far studied apparently show an increase, while others show a reduction in general death-rates following improvement in water supply. This is to be expected because of the numerous factors affecting the general and specific death-rates. The total death-rate shows a tendency

to decline in all the cities studied. This is also true of the death-rates from pulmonary tuberculosis, but is more marked in the control cities. The death-rates from pneumonia are quite irregular, but with a general downward tendency, except in Pittsburgh. The death-rates from nephritis show a gradual rise, except in one of the control cities, New York. No changes appear which are unique for the cities with improved water supplies. The curve for heart disease also shows a decline in New York, while in the other cities there is a rise. Considering the diseases that are sequelæ of typhoid fever as a whole, there is a general tendency toward an increase, but this is not peculiar to the cities which have had excessive typhoid fever rates. There can be no doubt that an impure water supply may be and, in general, is accompanied by a high general death-rate. Because of the multiplicity of factors involved, it is impossible to determine the exact relation between the two by a study of the general mortality statistics. Some cities will of necessity show a decrease, while others may even exhibit an apparent increase in mortality. That a high typhoid incidence tends to increase the number of deaths from the sequelæ of typhoid fever must also be true. But the large number of other factors tending to produce the same effect makes the problem very complicated, and one that probably cannot be solved by any comparison of mortality statistics.

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**Studies upon the Common House-fly (*Musca Domestica*, Linn).—**SCOTT (*Jour. Med. Research*, September, 1917, p. 121) made studies of the normal or "wild" *Musca domestica* in the District of Columbia since the autumn of 1913, and concludes that the common house-fly may carry pathogenic bacteria upon the surface of the body, legs, wings, and proboscides, mechanically, or they may carry infectious organisms in the intestinal tract and deposit them on foodstuffs, either in the "vomit spots" or in fecal deposits. The bacterial flora carried by the house-fly varies directly with the sanitation of the area in which the fly is captured, the most heavily polluted flies coming from the slum districts. House-flies show seasonal variation in the number of bacteria as well as in the species of bacteria. The seasonal variation shows the greatest bacterial flora is coincident with the summer months, and the occurrence of intestinal complaints of summer and early autumn. The isolation of members of the colon-typhoid-dysentery group of bacilli from numbers of flies indicates that the house-fly has the power of carrying the closely allied pathogens, typhoid and dysentery. The finding of virulent pyogenic cocci indicates the possibility of the common house-fly being a factor in the dissemination of the suppurative processes. The results of his experiments indicate that typhoid fever in the District of Columbia, under normal conditions, is not referable to the agency of the house-fly. The heavy bacterial flora and the presence of the intestinal group of bacteria on the house-fly presents a potent argument for the careful protection of foodstuffs from the access of flies, and furnishes a strong plea for the abolition of the breeding places of *Musca domestica*.

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**Epidemiology of Lobar Pneumonia.**—STILLMAN (*Jour. Exp. Med.*, October, 1917) reports that the results of his work confirm the previous observations of Dochez and Avery on the occurrence of healthy

carriers of disease-producing types of pneumococcus. Consideration of the results of study over a period of years showed that in the majority of instances, infection is due to organisms belonging to what Stillman calls Type I or Type II. The minority of cases, on the other hand, are due to so-called Types III and IV. Comparison of the types of pneumococcus obtained from the mouth secretions of normal persons with those isolated from individuals with lobar pneumonia shows the existence of two general classes of organisms. One of these, which consists of Types I and II, occurs only in association with disease. The other, which includes Types III and IV and the atypical Type II organisms, also causes pneumonia but these organisms are commonly found in healthy mouths. Rarely Types I and II have been found in the mouth secretions of normal individuals who give no history of association with cases of pneumonia. On the other hand, organisms of Types I and II have been found in 11 per cent. of normal individuals who have been in intimate association with a case of pneumonia of the same type. Although the presence of pneumococcus in dust has been known for some little time, little significance has been attached to it. The results of Stillman's work show that pneumococcus can be easily recovered from dust. The types of pneumococcus found reflect accurately the pneumococcus flora of the mouth of the members of these households. Pneumococcus of Types I and II is rarely found in dust except where a case of pneumonia due to the same type of pneumococcus has occurred. In view of the ease with which dust can be disseminated it is not surprising that in a few instances a Type I or Type II organism was recovered from the dust which did not correspond to the type of pneumococcus producing the disease. The occurrence of these disease-producing types of pneumococcus in the dust suggests the possibility that air-borne infection may play a part in the production of pneumonia. On the other hand, the mere presence of the disease-producing types of pneumococci in the mouth will not initiate disease. But if a susceptible individual comes in intimate contact with a case of pneumonia there is grave danger of his contracting the disease. These facts suggest the following conclusions concerning the epidemiology of lobar pneumonia. Infection with pneumococcus of Types I and II must be regarded as dependent upon either direct or indirect contact with a previous case of lobar pneumonia due to the same type of organism. These types of infection are either acquired by direct contact with a previous case of pneumonia, by association with a healthy carrier of one of these types of pneumococcus, or possibly by an air-borne infection from dust which has been infected. Infection with the sputum types of pneumococcus, namely, Types III and IV and the atypical strains of Type II, may be autogenic, or due to the acquisition by the individual of one of these types to which he is especially susceptible.

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ORIGINAL ARTICLES

A SOCIOLOGIC AND MEDICAL STUDY OF FOUR HUNDRED  
CIGAR WORKERS IN PHILADELPHIA.\*

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INTRODUCTION. About one year ago the Industrial Board of the Pennsylvania State Department of Labor and Industry asked the clinic for diseases of occupation of the University Hospital for some information which might help its members to decide whether or not children under sixteen years of age should be allowed to work in banding and packing rooms of cigar factories. A review of the literature upon the effects of tobacco work was unsatisfactory, and an investigation of the cigar industry in Philadelphia was therefore planned, including a survey of the hygienic conditions of some of the factories and an intensive study of a limited number of employees. The former study appears in a separate communication,† while this one presents a review of the literature and a study of the social and medical histories and the physical examinations of 400 workers in that industry.

LITERATURE. In the first treatise upon the diseases of tradesmen, written by Ramazzini<sup>1</sup> in the latter part of the seventeenth

\* Read before the Philadelphia County Medical Society.

† Smyth and Miller: A Hygienic Survey of Cigar Manufacturing in Philadelphia, Med. and Surg., September, 1917.

century, a chapter was devoted to tobaccoists or those who made snuff. The author recognized among them nervous, gastro-intestinal, and respiratory disturbances, and since his time the genital and circulatory systems have been included among those described as being affected injuriously by tobacco work. The extent of the injury done by tobacco has, however, been a disputed problem since Ramazzini's time, and the controversy has called forth numerous publications, particularly in the last half-century. Some of the writers, including Duchatalet,<sup>2</sup> Thackrah,<sup>3</sup> and Arlidge,<sup>4</sup> denied any injurious influences, while Schwabe<sup>5</sup> and Piasecki<sup>6</sup> even ventured to say that working in tobacco was healthful. Rochs<sup>7</sup> believed that the work in sufficiently ventilated rooms was harmless, while Oliver<sup>8</sup> found nothing in the French, Spanish, or British factories to lead him to regard it as an occupation dangerous to health, and Rambousek<sup>9</sup> stated as late as 1913 that the industrial poisoning from tobacco was not proved. On the other hand, Merat<sup>10</sup> believed that tobacco factories were incubators for serious disease conditions, and Rosenfeld,<sup>11</sup> who made a careful study in 1889 of the Austrian statistics, including 35,164 workers from twenty-eight factories, found high morbidity and mortality rates. Kober<sup>12</sup> stated that a lowering of general resistance resulted from this work.

The respiratory system seems to have attracted most attention. Ramazzini<sup>1</sup> spoke of the workers sneezing, and of the horses, which were used to grind the tobacco into dust, coughing and blowing their nostrils. Melier,<sup>13</sup> in 1844, spoke of a transitory bronchitis among tobacco workers, but claimed that the work arrested tuberculous disease, as did also Reuf.<sup>14</sup> Hirt<sup>15</sup> described an irritation of the bronchial, nasal, and conjunctival mucous membranes in beginners at this work, but found no tendency to chronic catarrh, chronic pneumonia, emphysema, or tuberculosis. He exposed rabbits and dogs to tobacco dust for several months, but was never able to provoke any signs of catarrh or a loss of appetite, although at autopsy some brownish spots and some atrophic areas were found in their lungs. Merkel,<sup>16</sup> in 1882, found fine brown spots in the lungs of tobacco workers, and after this there were many reports of lung diseases, particularly tuberculosis. Rosenfeld<sup>11</sup> stated that tuberculosis was the disease of the tobacco worker, finding 1.73 per cent. of the Austrian workers to be tuberculous, whereas the percentage among factory workers in general was only 1.25, and Schellenberg<sup>17</sup> found that the tuberculosis death-rate of cigar workers in one town of Baden between 1887 and 1893 ranged between 1.77 and 2.7 per cent., whereas for the total population during the same period it was 0.27 to 0.29. Stephani<sup>18</sup> found a high tuberculosis morbidity rate as well, and Abelsdorf<sup>19</sup> declared that women were affected more frequently than men.

Hoffman<sup>20</sup> showed that the United States statistics for 1909 gave cigar makers and tobacco workers a higher death-rate from all

causes in each age group than they did the manufacturing and mechanical class or the mercantile and trading class. He presented tables for comparisons, by age groups, of the total and the tuberculosis mortality of tobacco workers with that of all occupied workers in England and Wales (1900 to 1902), which, on the whole, gave the tobacco workers a higher percentage. In some age groups, however, the reverse was true, and in Switzerland (1871 to 1890), according to statistics which he also presented, the tuberculosis mortality for tobacco workers under forty years was less than for all occupied males. He was able to show finally that the proportionate mortality from consumption among 141 tobacco workers (1897 to 1906), as indicated by the figures of an industrial insurance company, was 38.8 per cent. against 14.8 per cent. for all males in the registration area of the United States (1900 to 1906), and that the proportionate mortality from consumption among 1530 cigar-makers and packers (1897 to 1906) was 28.9 per cent. against the same 14.8 per cent. His conclusion, based on a study of the literature and the above figures, was that tobacco workers were subject to an excessive mortality from consumption and from other respiratory diseases.

Kober<sup>12</sup> has stated that recent United States statistics show that among twenty-three occupations tabulated cigarmakers and tobacco workers occupy second rank in mortality from tuberculosis. The proportionate mortality from tuberculosis of the lungs among cigarmakers and tobacco workers compared with that in all occupations and in other specified occupations in the registration states (1909), by age groups, is presented in Table I.<sup>21</sup>

TABLE I.

Age at death, years.	Cigar and to- bacco workers.	Physicians and surgeons.	Marble and stone-cutters.	Printers.	All occupations.
25 to 34 . .	49.3	21.2	46.7	51.5	31.0
35 to 44 . .	33.7	15.8	41.0	32.6	23.6
45 to 54 . .	23.2	9.2	42.9	22.3	14.4

The gastro-intestinal symptoms of tobacco workers were emphasized by Thiele,<sup>22</sup> who claimed that the volatile oil and the nicotin of tobacco irritated the throat, producing cough, nausea, and vomiting. Nausea, diarrhea, and increase in gastric acidity were spoken of in Ramazzini's<sup>1</sup> original paper, while Chapman<sup>23</sup> described abdominal pain, constipation, and collapse. Rosenfeld<sup>11</sup> found 11.6 per cent. of the Austrian tobacco workers to be suffering from some gastro-intestinal disturbance, whereas the percentage for textile workers was 8.5, and Jehle<sup>24</sup> found similar disturbances in 20.7 per cent.

of tobacco workers, but in only 11 per cent. of other workers. Thompson<sup>25</sup> described gastro-intestinal as well as nervous and vascular symptoms, but did not rate the occupation as especially hazardous.

Anemia has been considered by many to be a result of tobacco work, and Rosenfeld<sup>11</sup> suggested a specific action of tobacco in its production. He found anemic 1.92 per cent. of cigar workers as against 0.77 per cent. of all workers, and Jehle<sup>24</sup> found 7.81 per cent. of tobacco workers with anemia, while other workers showed only 2.81 per cent. Thiele<sup>22</sup> and Bresler<sup>26</sup> believed that these workers suffered from anemia, and the latter attributed their pelvic disturbances to this condition.

Menorrhagia was noted among tobacco workers by Patisier, Richardson, James, Kostial, Morat and Brodie, according to the New York Factory Investigating Commission,<sup>27</sup> and Rosenfeld<sup>11</sup> claimed that menstrual disorders were twice as frequent in these as in other workers; but Poisson,<sup>23</sup> Joire,<sup>29</sup> Piasecki,<sup>5</sup> and Oliver,<sup>8</sup> did not regard tobacco as an emmenagogue. Petit,<sup>30</sup> however, was able constantly to produce anatomical changes in the genital organs of animals by feeding them with tobacco, and Guillain and Gy<sup>31</sup> produced abortions in animals by the same means. In further support of its abortifacient effect Rosenfeld<sup>11</sup> found the percentage of miscarriages higher than in other women, while Emerson and Tracy<sup>32</sup> found the number of children in the families of tobacco workers quite small. Bresler<sup>26</sup> stated that it was known girls sought work in tobacco factories in order to bring about a termination of pregnancy, and Robinson<sup>33</sup> claimed that the most trifling genital lesion was enough to bring about an abortion in a tobacco worker. These facts suggested to Abelsdorf<sup>18</sup> that nicotin had a specific abortifacient effect, but Etienne,<sup>34</sup> Piasecki,<sup>5</sup> Ygonin,<sup>35</sup> Thiele,<sup>22</sup> and Oliver<sup>36</sup> believed that tobacco had no such influence. Etienne,<sup>34</sup> however, found the infant mortality to be twice that of other families, and he as well as Kostial<sup>37</sup> and Abelsdorf<sup>18</sup> suspected that this was due to the presence of nicotin in the mother's milk. Oliver,<sup>36</sup> on the other hand, stated that in Madrid he saw women leave their work at a certain hour to suckle their children, and that it would be difficult to see stronger and better nourished babies anywhere.

Among the nervous symptoms mentioned by Ramazzini<sup>1</sup> were headache, migraine, and squeamishness, and he supposed that the brain was clouded and narcotized. Thiele<sup>22</sup> added dizziness, sleeplessness, fatigue, heaviness of the hands and feet, and hyperesthesias to this category of nervous symptoms. Strümpell<sup>33</sup> described a nicotin tabes. Caparelli<sup>39</sup> reported as a result of an intensive study of twenty-five workers in tobacco fermenting rooms a heightened blood-pressure and an influence upon cardiac rhythm.

THE CIGAR INDUSTRY IN PHILADELPHIA. During the fifteen-year period (1899 to 1914) 130 establishments for the manufacture

of tobacco products in Philadelphia either shut down or combined with other plants, but during the same time the number of employees and the value of the products increased, as Table II shows. This was due to the organization of large companies and their ability to buy the raw material and produce the cigars more economically, thus forcing out the small companies and the individual manufacturers.

TABLE II.—MANUFACTURES OF TOBACCO, CIGARS, AND CIGARETTES IN PHILADELPHIA.

Census.	Number of establishments.	Number of employees.	Total value of products.
1899 <sup>40</sup> . . . . .	556	6960	\$8,991,000
1904 <sup>40</sup> . . . . .	617	6710	8,655,000
1909 <sup>40</sup> . . . . .	496	7634	13,429,000
1914 <sup>41</sup> . . . . .	426	7982	12,733,281

If the proportion of cigar workers among all the tobacco employees of the city in 1914 was the same as that given by the 1905 census of manufactures for the entire United States there were in that year 6512 of the former in Philadelphia, and the number has probably changed very little in the past two years. Almost one-half of this number, 3199, were employed in the seven factories in which we made the examinations here reported, and a greater number are included in our paper upon the hygiene of the industry. Only 400 of these, however, were subjected to our study, and they were distributed among the factories, according to processes, as is shown in Table III. A detailed description of these processes is given in the paper by Smyth and Miller.

TABLE III.—DISTRIBUTION AMONG EMPLOYERS BY SEXES AND BY PROCESSES.

Employer.	Males.				Females.				All workers.
	Cigar-makers.	Packers.	Driers.	Casers.	Cigar-makers.	Packers.	Strip-pers.	Banders.	
T. . .	33	12	11	9	23	11	11	3	113
S. . .	2	4	0	0	34	13	0	6	59
M. . .	0	0	0	0	0	33	20	0	53
B. . .	0	0	3	0	0	5	0	5	13
J. . .	0	0	0	0	19	9	18	0	46
L. . .	17	2	0	0	19	2	0	0	40
R. . .	5	0	0	0	62	0	2	7	76
Total	57	18	14	9	157	73	51	21	400

MODE OF INVESTIGATION. Although the method of conducting this investigation did not differ fundamentally perhaps from that of similar studies in other industries a statement of it is deemed



appropriate. From a list<sup>42</sup> of 160 establishments for the manufacture of cigars in the city we selected 25 of the larger ones, and by means of a circular letter requested their coöperation in this study. These factories were then visited and the nature of our proposed investigation more fully explained. When we were able to talk to the superintendents or to employers who had themselves grown up in the business we found a ready welcome and a desire to coöperate; when, however, employers who had not had actual experience as employees in the industry were encountered some objections were raised, the chief one being that the employees would not permit such a study. In a few of these instances, however, a trial was permitted, and in these, as in all the factories where we once came into contact with the workers, we had no further difficulties.

The employers were in every instance most courteous, and our hearty thanks are due them for the facilities which they put at our disposal. The superintendents always brought the matter to the attention of the workers, and, as a rule, only a few would consent to the examination at first; but after a start was made there was little difficulty in seeing as many as we could examine. Our plan was for the social service worker<sup>43</sup> to see the subject first and to elicit the social and industrial history, and then to pass the worker on to the examiner, who in turn procured the medical history and made as complete a physical examination as was possible. In many instances this meant an examination of the entire body, but sometimes it meant, on account of the semipublicity of the examining room, that the lower chest and abdomen had to be omitted. Fifteen to thirty minutes were required for each individual. Blood-pressure readings were taken and urines and blood smears examined when there was any suspicion of abnormality, while on about 100 girls the blood-pressure was determined routinely, and blood smears from 50 consecutive subjects were studied.

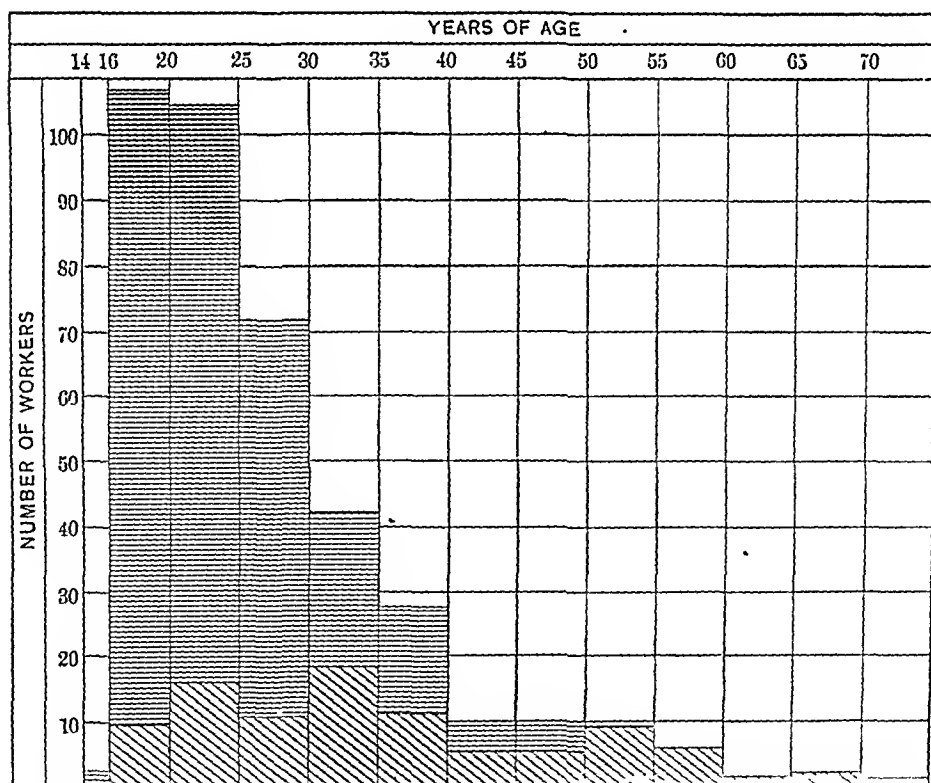
ANALYSIS OF DATA UPON WORKERS. *Sexes and Ages.* Of the 400 cigar workers included in this study 98 were males and 302 were females. Of the latter 157 were cigarmakers,\* 73 packers, 51 strippers,† and 21 banders; whereas of the males, 57 were cigarmakers, 18 packers, 14 driers, and 9 casers. Table IV shows that 54.2 per cent. of them were under twenty-five years of age and 82.7 per cent. under 35. This large proportion in the early age groups is due to the female workers, since 63.5 per cent. of them were under twenty-five and 92.1 per cent. under thirty-five, while only 25.5 per cent. of the males were under twenty-five and 54.1 per cent. under thirty-five. This is shown graphically in the Chart.

\* In this group of cigarmakers are included both bunch makers and rollers and both machine and hand workers.

† Applies to selectors and strippers together.

TABLE IV.—PERCENTAGE OF DISTRIBUTION, BY AGE GROUPS,  
ACCORDING TO SEXES AND PROCESSES, AND FOR ALL  
WORKERS.

Years.	Males.					Females.					All work- ers.
	Cigar- makers.	Pack- ers.	Dri- ers.	Cas- ers.	Total.	Cigar- makers.	Pack- ers.	Strip- pers.	Band- ers.	Total.	
14-15	..	..	..	..	..	..	4.1	..	..	0.9	0.7
16-19	12.3	5.6	7.1	..	9.2	26.7	38.4	39.3	42.9	32.8	27.0
20-24	14.0	33.4	14.3	..	16.3	36.4	28.7	13.7	23.8	29.8	26.5
25-29	12.3	5.5	7.2	11.1	10.2	21.6	20.5	17.6	14.3	20.3	17.8
30-34	24.5	11.1	7.1	11.1	18.4	9.6	5.5	7.8	9.5	8.3	10.7
35-39	12.2	5.0	14.3	22.2	12.3	3.2	2.8	11.8	4.8	4.6	6.5
40-44	5.3	5.6	7.2	11.2	6.1	1.3	..	3.9	..	1.3	2.5
45-49	5.3	5.0	7.1	11.1	6.1	0.6	..	3.9	4.7	1.3	2.5
50-54	5.3	16.7	14.3	11.1	9.2	..	..	2.0	..	0.3	2.5
55-59	1.8	11.1	7.2	22.2	6.1	..	..	..	..	..	1.5
60-64	1.8	..	7.1	..	2.0	..	..	..	..	..	0.5
65-69	3.5	..	7.1	..	3.1	..	..	..	..	..	0.7
70-74	..	..	..	..	..	0.6	..	..	..	0.4	0.3
Unkn.	1.7	..	..	..	1.0	..	..	..	..	..	0.3
Total	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
No.	57	18	14	9	98	157	73	51	21	302	400



Number of workers in age groups by sexes. The oblique lines represent males and the horizontal lines females.

*Length of Employment.* The average duration of employment in the industry would then be expected to be much greater for the males, and Table V shows this to be the case. The single longest stay in the trade, however, was that of a woman who had worked as a cigarmaker for sixty-five years. The number of years of employment in the particular factory in which examined also averaged greater for the males. The cigarmakers had been longer in the industry than the workers in any other process, with the packers occupying second position among the males and the strippers among the females. Since these are the processes requiring the greatest amount of skill it is but natural that the workers should have stayed longest in them.

TABLE V.—AVERAGE LENGTH OF TIME IN THE INDUSTRY AND IN THE FACTORY IN WHICH EXAMINED.

Years.	Males.					Females.				
	Cigar-makers.	Packers.	Drivers.	Casers.	Average.	Cigar-makers.	Packers.	Strippers.	Banders.	Average.
In the industry . . .	17.0	14.6	11.8	7.3	14.8	6.9	4.4	6.8	5.1	6.3
In the factory in which examined . . .	5.2	5.8	8.4	2.2	5.3	2.6	3.4	2.7	3.0	2.8

*Nativity.* A tabulation of the nativity records shows that more than half, 55.5 per cent., were born in the United States, although among 14,356 cigar workers in this country in 1913 only 21.09 per cent. were American.<sup>42</sup> Russia and Austria-Hungary were the most frequent native countries of the foreign-born, and with America included 81 per cent. of the total. Of their fathers only 24.7 per cent. were born in the United States, and of their mothers 26.5 per cent., yet the order of frequency of the birthplace of the parents followed roughly that of the workers, except that Germany occupied a relatively higher position with the parents, and that Ireland, Belgium, Bulgaria, Spain, and Switzerland were represented among the parents but not among the workers themselves. According to religion Roman Catholics predominated with 45.2 per cent.; Protestants and Jews being about equally divided among the others.

*Civil Condition.* An analysis of the civil or conjugal condition reveals that 60.5 per cent. were single, and this is to be explained by the preponderance of the subjects in the early age groups. The older ages of the men accounted for 63.2 per cent. of them being married, whereas only 29.5 per cent. of the females were or had been married. These figures may be compared with those for 13,743 cigar workers in this country in 1913, among whom 57.88 per cent.

of the males were married and 20.11 per cent. of the females.<sup>42</sup> Among the women more of the strippers than of any of the other process groups were married, and this also is due to their older age distribution.

*Earnings and Hours of Work.* Piece rates prevailed with all the employees except the driers and casers, and the differences in the earnings of the sexes were slight. The cigarmakers of the seven factories averaged \$14 to \$18 per week of fifty-four hours, the packers \$16, the driers \$10 to \$11, the casers \$14, the strippers \$8 to \$10, and the banders \$9 to \$10. It was not uncommon to find a cigarmaker earning \$25 per week, and one young girl who did machine-cigarmaking earned \$30 regularly. These figures are in strong contrast with those presented by the United States Commissioner of Labor<sup>44</sup> in 1913, when as the result of the compilation of statistics for 13,565 cigar workers, including those from nine factories in Pennsylvania, he stated that half of the females and one-twelfth of the males earned under \$6 per week, and that only one-tenth of the women and three-fourths of the men made over \$10 per week. In addition to the large increase in all wages since that time it is probable that a better grade of cigars are made and consequently better wages are paid in the factories here considered than in the industry generally.

In this connection, too, it is to be remembered that many of the workers whom we studied seldom did full-time work of nine and three-quarter hours per day and fifty-four hours per week. The packers never work late in the afternoons or on dark days because of inadequate light, and it is the habit of some workers in other processes to come late in the mornings, to take extra time at the lunch period, and at times to leave early in the afternoons. Some do this because of home duties and others only because they are allowed to. It is of interest that some of the best-paid employees were these short-day workers.

*Menstruation and Fecundity.* The great divergence of opinion and the paucity of actual data in the literature on the effect of tobacco work upon the menstrual function indicated the importance of careful questioning in regard to this matter. Among 296 females so questioned we secured a history of dysmenorrhea in 42, of menstrual irregularities in 17, and of menorrhagia in only 2, while in 232 we obtained perfectly normal histories. These facts, with those for the individual processes, are presented in percentages in Table VI. It will be observed that in each group at least 75 per cent. of the histories were normal, thus suggesting that tobacco does not have a harmful influence upon this function.

The claim which has been made repeatedly, and which was apparently supported by Emerson and Tracy's<sup>33</sup> findings in New York, that women who work in tobacco give birth to few children, also suggested some inquiries along this line. Among 93 married

women we found only 50 who had ever given birth to a child, 53.8 per cent. (Table VII). The total number of children was only 95, this meaning an average of less than two to each mother and of about one to each married woman. Emerson and Tracy found in one group of 58 families an average of  $1\frac{1}{2}$  to a family, and in another group of 53 families  $1\frac{3}{4}$  to a family. While these figures seem convincing, they may at the same time be misleading, inasmuch as the superintendents whom we questioned about this were of the opinion that the cause lay in the frequent use among these people of means for the prevention of conception and in induced abortions. Furthermore, they were able to tell us of many families in which the mother worked in tobacco and in which there were the usual number of children. It will be noted that the statements of miscarriages, as also presented in Table VII, are not excessive.

TABLE VI.—MENSTRUAL HISTORIES OF 296 FEMALE WORKERS  
ACCORDING TO PROCESSES AND AS A WHOLE, IN  
PERCENTAGE AFFECTED.

Condition.	Cigar-makers.	Packers.	Strippers.	Banders.	All workers.
Dysmenorrhea . . . . .	13.5	12.7	16.3	20.0	14.2
Irregularities . . . . .	7.7	4.2	..	10.0	5.7
Amenorrhea . . . . .	2.6	2.8	2.0	..	2.4
Menorrhagia . . . . .	..	..	4.1	..	0.7
Normal . . . . .	77.0	83.0	77.5	75.0	78.4
Number . . . . .	156	71	49	20	296

TABLE VII.—FECUNDITY OF 93 MARRIED WOMEN ACCORDING TO  
PROCESSES AND AS A WHOLE.

	Cigar-makers.	Packers.	Strippers.	Banders.	All workers.
Number . . . . .	51	12	24	6	93
Percentage having borne children .	55.0	50.0	50.0	66.6	53.8
Average number of children per married woman . . . . .	1.08	0.83	1.0	1.0	1.02
Average number of children per mother . . . . .	1.96	1.67	2.0	1.5	1.9
Average number of miscarriages per married woman . . . . .	0.31	0.08	0.04	0.17	0.2

PAST MEDICAL AND OPERATIVE HISTORY. The past medical histories revealed only that these workers had suffered from the usual diseases of childhood and adolescence. Measles had occurred in 55 per cent. of them, tonsillitis in 24, whooping-cough in 22.7, mumps in 19.2, and typhoid fever in 11 per cent. Influenza, scarlet fever, and diphtheria had each occurred in a little more than 10 per cent. Only the men were questioned as to gonorrhea and syphilis, and of these 12 admitted the Neisserian infection and 3 lues. The past operative histories indicated that tonsillectomies

and appendectomies were most frequent, and that the proportion of operations upon the men was less than half that upon the women. Among the latter there were 6 laparotomies for pelvic conditions and 6 uterine dilatations and curettements.

*Weights and Measurements.* The weights and certain anthropometric measurements were secured in each individual and the averages of these for the workers in each process, by sexes, together with general averages for each sex, are presented in Table VIII. It is appreciated that these figures are of little value except as they may be compared with similar observations upon workers in other industries, and it is hoped that we may at some time have such data upon all occupations.

TABLE VIII.—AVERAGE ANTHROPOMETRIC WEIGHTS AND MEASUREMENTS, BY SEXES, IN EACH PROCESS WITH GENERAL AVERAGES.\*

	Males.					Females.				
	Cigar-makers.	Packers.	Driers.	Casers.	Average.	Cigar-makers.	Packers.	Strippers.	Banders.	Average.
Weight . .	62.4	64.9	64.1	67.1	63.5†	58.0	54.8	61.0	56.6	57.6†
Height . .	169.6	169.1	169.0	166.0	169.3†	160.6	162.7	161.1	159.3	161.2†
Breadth of shoulders	38.2	39.2	39.1	39.6	38.7	36.2	35.9	36.9	36.1	36.2
Breadth of chest . .	26.5	26.9	27.3	28.3	26.9	25.3	24.6	24.3	25.5	25.0
Breadth of waist . .	25.4	25.8	27.2	28.2	26.0	22.3	21.6	22.8	22.0	22.2
Breadth of hips . .	32.1	32.1	33.7	33.8	32.5	34.1	33.3	34.0	33.0	33.8
Depth of chest . .	19.4	19.4	20.9	21.7	20.0	18.3	18.5	17.2	18.8	18.2
Depth of abdomen . .	19.1	19.8	20.5	22.0	19.9	18.0	18.2	18.1	18.5	18.1
Girth of neck . .	35.1	35.2	35.7	34.9	33.0	31.7	31.1	32.0	31.2	31.6
Girth of chest contracted	84.8	85.1	91.7	89.5	86.1	80.8	79.4	80.8	82.7	80.6
Girth of chest expanded	91.2	92.0	97.0	94.6	92.4	85.8	85.5	87.3	87.3	86.1
Girth of waist . .	77.7	79.3	83.5	83.6	79.3	70.3	69.2	75.2	70.0	70.9
Girth of hips	92.3	94.2	96.6	93.9	93.9	97.5	95.1	102.6	97.0	97.7
Number . .	57	18	14	9	98	157	73	51	21	302

*Build, Posture, Nutrition and Development.* In regard to build, posture, nutrition, and development it is possible to record only the examiner's impressions, and these are figured in Table IX. It will be noted that in each instance the figures are better for the women than the men, but it must not be forgotten that the men

\* Weights are expressed in kilograms and measurements in centimeters.

† 63.5 kg. = 140 pounds; 57.6 kg. = 127 pounds; 169.3 cm. = 66.7 inches; 161.2 cm. = 63.4 inches.

represent older age groups. Attention is also called to the fact that the driers and casers have the poorest build and posture but the best development; the explanation probably lies in their doing heavier manual labor than the others.

TABLE IX.—BUILD, POSTURE, NUTRITION AND DEVELOPMENT IN PERCENTAGE OF THE WORKERS IN THE SEVERAL PROCESSES, IN EACH SEX, AND IN THE TOTAL NUMBER.

### BUILD.

	Males.					Females.					Total.
	Cigar-makers.	Pack-ers.	Driers.	Casers.	Total.	Cigar-makers.	Pack-ers.	Strip-pers.	Band-ers.	Total.	
Good	56.2	53.0	46.2	44.4	53.1	55.7	64.4	70.6	66.6	61.1	59.2
Fair	42.1	29.4	46.2	44.4	40.7	43.0	34.2	27.4	33.4	37.6	38.3
Poor	1.7	17.6	7.6	11.2	6.2	1.3	1.4	2.0	..	1.3	2.5
Total	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0

### POSTURE.

Good	63.1	61.1	35.7	44.4	57.2	71.2	72.2	60.8	76.2	70.0	66.8
Fair	19.3	22.2	21.4	33.4	21.4	21.8	22.2	31.4	23.8	23.7	23.1
Poor	17.6	16.7	42.9	22.2	21.4	7.0	5.6	7.7	..	6.3	10.1
Total	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0

### NUTRITION.

Good	52.6	50.0	69.2	66.6	55.1	65.6	67.1	68.7	66.6	66.5	64.0
Fair	42.1	33.3	23.1	33.4	37.1	24.8	30.1	25.5	33.4	26.8	29.3
Poor	5.3	16.7	7.7	..	7.2	9.6	2.8	5.8	..	6.7	6.7
Total	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0

### DEVELOPMENT.

Good	50.9	37.5	92.3	87.5	56.8	61.0	59.4	60.8	81.0	62.0	60.7
Fair	42.1	56.3	7.7	12.5	36.9	37.1	33.4	35.2	19.0	34.6	35.2
Poor	7.0	6.2	..	..	6.3	1.9	7.2	4.0	..	3.4	4.1
Total	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
No.	57	18	14	9	98	157	73	51	21	302	400

*Physical Findings.* The physical findings in percentages for the various groups are set forth in Table X. Congestion of the conjunctival mucous membrane was most frequent, and it was of such a grade as to suggest some cause inherent in the industry as at present conducted. It was observed that those who wore glasses were not so frequently affected, and this indicated a method by which this finding could be obviated. This subject will be amplified in a subsequent publication by T. B. Holloway, who made careful and exhaustive studies upon the eyes of some of these workers.

TABLE X.—PHYSICAL FINDINGS IN WORKERS, IN PERCENTAGE, ACCORDING TO SEXES AND PROCESSES AND AS A WHOLE.

	Males.					Females.					All work-ers.
	Cigar-makers.	Packers.	Driers.	Casers.	Total.	Cigar-makers.	Packers.	Strippers.	Banders.	Total.	
Conjunctival congestion . . .	65.4	72.2	64.4	77.8	64.4	46.6	67.1	64.8	76.2	56.6	58.5
Dental caries . . .	36.6	39.0	93.0	77.8	47.0	33.1	38.4	45.1	38.1	36.8	39.2
Dental wearing . . .	54.0	16.7	28.6	33.4	38.8	40.8	..	15.7	..	23.9	27.5
Dental insufficiency . . .	17.3	27.8	50.0	55.6	26.6	11.5	21.9	15.7	14.3	14.8	17.7
Pyorrhea . . .	15.4	33.4	71.5	22.2	26.6	8.9	..	7.8	4.8	6.3	11.2
Tremors of eyelids	19.2	33.4	7.1	33.4	20.4	40.8	54.8	43.2	28.6	43.7	38.0
Palpable glands:											
Axillary . . .	55.8	72.2	52.2	55.6	56.2	31.8	23.3	3.9	23.8	24.5	32.2
Cervical . . .	30.8	39.0	42.9	33.4	32.7	13.4	27.4	9.8	4.8	15.6	19.7
Epitrochlear . . .	36.6	39.0	42.9	55.6	37.8	1.3	1.4	..	4.8	1.3	10.2
Pharyngeal congestion . . .	38.4	50.0	71.5	33.4	42.9	14.0	11.0	31.4	..	15.2	22.0
Tonsils:											
Diseased . . .	11.5	11.1	14.3	..	10.2	17.8	9.6	15.7	19.0	15.6	14.2
Enlarged . . .	5.8	5.6	7.1	11.1	6.1	21.7	9.6	7.8	9.5	15.6	13.2
Hyperactive reflexes . . .	5.8	..	..	..	3.1	7.6	32.9	11.8	9.5	14.6	11.7
Lungs: suspicious infiltration:											
Right apex	11.5	16.7	21.4	..	12.3	8.3	16.4	11.8	14.3	11.3	11.5
Left apex	3.8	5.6	..	..	3.1	1.3	2.7	2.0	4.8	1.9	2.2
Apical fibrosis	1.9	5.6	7.1	..	3.1	1.3	..	2.0	..	1.0	1.5
Emphysema . . .	5.8	..	14.3	..	5.6	0.6	..	..	..	0.3	1.5
General fibrosis	3.8	5.6	..	22.2	5.6	..	..	..	..	..	1.2
Thyroid fulness . . .	..	..	..	..	..	5.7	12.3	3.9	14.3	7.6	5.7
Heart:											
Mitral murmur:											
Systolic . . .	..	..	28.6	22.2	6.1	2.5	9.6	2.0	9.5	4.6	5.0
Presystolic . . .	..	..	..	..	..	0.6	..	3.9	..	1.0	0.7
Aortic systolic murmur . . .	..	..	..	..	..	..	..	..	4.8	0.3	0.2
Pulmonic murmur . . .	..	..	..	..	..	..	4.1	3.9	..	1.7	1.2
Weak heart sounds . . .	11.5	5.6	..	..	7.1	1.3	..	..	9.5	1.3	2.7
Arrhythmia . . .	..	..	..	..	..	0.6	4.1	3.9	..	2.0	1.5
Arteriosclerosis . . .	11.5	5.6	21.4	..	10.2	..	..	..	..	..	2.5

Various dental abnormalities occupy second place in our classification. There were 157 who showed gross dental caries, and 110, or 27.5 per cent., presented a wearing away of the biting and grinding surfaces of all their teeth, such as is seen in men who have chewed tobacco for a long time. It is interesting that this occurred in the females as well as in the males, but that among the women it was seen only in those working in processes in which tobacco could be placed in the mouth, the cigarmaking and stripping departments. The banders and packers handle only finished cigars and so have no opportunity of getting tobacco into the mouth,



and none of the females in these processes showed dental wearing. Among the men instances were found in every process, but the men handle raw tobacco in all their departments, and even when their teeth do not aid them in their skilled work they keep tobacco in their mouths. Some, even of the girls, after a year or less of work in tobacco will show this dental wearing; and some of those who have worked five or more years and who constantly use their teeth show the latter worn almost half down to the gum margins. The tobacco contains a certain amount of gritty material, sand and organic matters, and it seems likely that enough of this gets upon the teeth, even by licking the binders and wrappers, to slowly grind down the biting and chewing surfaces when they are approximated, as might emery. A second factor in its production may be simply the biting together of the teeth, as in biting out bunches. Seventy-one of the workers showed what we have arbitrarily termed an insufficiency of teeth, indicating a loss of five or more. Pyorrhea was present in 11.2 per cent.

Because of the significance which some clinicians attach to tremors of the eyelids when lightly closed as indicative of neurotic conditions data were secured upon the presence of this phenomenon, showing 38 per cent. to be so affected. Hyperactive reflexes might be expected to correspond roughly with the presence of these tremors if they are suggestive of a neurotic state, but were found in only 11.7 per cent.

The pharynx was congested in 22 per cent., and in some it was quite dry and glistening. As many of the workrooms have a low humidity with a somewhat high temperature, and as tobacco dust is quite hygroscopic, this finding is readily explained. The banders work in the cleanest, the least dusty, and the best ventilated rooms, as is shown by Smyth and the writer, and among these there was not found a single instance of pharyngeal catarrh.

Abnormal tonsils were discovered in 27.4 per cent. of the employees examined. In 13.2 per cent. the tonsils were simply enlarged, while in 14.2 per cent. they were cryptic and diseased.

It is very difficult to differentiate between normal and slightly abnormal findings in the lungs, and if we have erred in this regard we believe that it has been in placing too many in the abnormal or doubtful class. Although the predominance of right-sided apical lesions presented in our table suggests that we have done this, our figures nevertheless represent our impressions at the times of the examinations. We found 46 with what we considered slight right apical pulmonary infiltration and 9 with the same on the left side. In none of these did we get rales and none had sputum. In 6 other instances the signs of old inactive apical infiltration were unquestionable, 3 in males and 3 in females. Emphysema was noted 6 times, and signs of a general fibrosis 5 times; all the latter were men.

Heart examinations revealed a mitral systolic murmur in 20 instances, weak heart sounds in 11, an arrhythmia in 6, a pulmonic

systolic murmur in 5, a mitral presystolic murmur in 3, and 1 aortic systolic murmur. In no case was decompensation present. No instances of marked arteriosclerosis were detected, but a few of the workers showed it in mild degree.

Blood-pressure studies were made upon 147 employees, using the auscultatory method, and the averages are presented in Table XI. The lowest average systolic reading for any group was 118 for the female cigarmakers and the highest 131 for the casers. All the diastolic averages ranged between 73 and 85.

TABLE XI.—BLOOD-PRESSURE AVERAGES ON 147 WORKERS.

	Males.					Females.				
	Cigar-makers.	Packers.	Driers.	Casers.	Total.	Cigar-makers.	Packers.	Strippers.	Banders.	Total.
Number studied . . .	30	14	11	9	64	78	33	27	9	147
Average systolic pressure . . . . .	124	130	130	131	128	118	121	127	127	121
Average diastolic pressure . . . . .	80	82	80	73	81	78	82	85	74	81

*Diagnosis.* Some of the physical conditions presented in Table X, such as dental caries and diseased tonsils, constitute in themselves diagnoses, but others can be so interpreted only in the light of the clinical history and examinations in the individual worker. The latter conditions, such as pulmonary infiltration and thyroid fulness, have been reconsidered in this light and in those instances where diagnoses seemed justified they were recorded and are presented separately in Table XII. This table also includes such other diagnoses as we have been able to make. Because of our limited study some of these are only symptoms, but insofar as possible we are presenting etiological diagnoses.

Chronic constipation stood first among the diagnoses, being present in 19.2 per cent. of the total number. It was most frequent in the females, and among them most often in the cigarmakers and the strippers. The packers, who stand constantly at their work, showed only a slightly lower percentage than the strippers among the females, but there was none among the male packers. The banders showed the lowest percentage, although they sit at their work.

Headaches, exclusive of those due to menstrual or other transient conditions, were complained of 45 times. Among the females 13.7 per cent. suffered in this way as against 5.1 per cent. among the males. Some of them were no doubt due to eye-strain, as was suggested by several of the girls telling us of similar headaches which they had had and which disappeared after they had been glassed. All of these workers with obscure headaches were advised to secure eye examinations; and we have records of a few in which

this was done and refractive errors were found. It is possible that some of the headaches were due to fatigue or the toxic effect of tobacco, but of this we have no proof.

TABLE XII.—DIAGNOSES, ACCORDING TO SEXES AND PROCESSES, IN PERCENTAGE OF WORKERS AFFECTED.

Diagnoses.	Males.				Females.				All workers.
	Cigar-makers.	Packers.	Drivers.	Cases.	Cigar-makers.	Packers.	Strippers.	Banders.	
Constipation . . . . .	8.8	..	7.1	22.2	31.2	15.1	15.7	4.8	19.2
Apparently normal . . . .	12.3	16.7	..	11.1	8.9	16.4	21.6	4.8	12.2
Headache . . . . .	7.0	..	7.1	..	13.4	5.5	7.8	52.4	11.2
Gastric neurosis . . . . .	3.5	..	14.3	22.2	11.5	4.1	2.0	..	7.0
Neurasthenia . . . . .	3.5	5.6	..	..	7.0	2.7	4.0	..	4.4
Slight hypertension . . . .	..	5.6	..	..	0.6	8.2	5.9	4.8	3.0
Pelvic inflammation . . . .	..	..	..	..	3.2	4.1	7.8	..	3.0
Secondary anemia . . . . .	..	..	..	..	3.8	1.4	5.9	..	2.5
Backache . . . . .	3.5	..	..	..	1.3	..	..	9.5	1.5
Conjunctivitis . . . . .	..	..	7.1	..	1.9	..	..	9.5	1.5
Arrested pulmonary tubercu- losis . . . . .	1.8	5.6	7.1	..	1.3	..	2.0	..	1.5
Questionable active pulmo- nary tuberculosis . . . . .	1.8	5.6	..	..	1.3	2.7	..	..	1.2
Vasomotor neurosis . . . .	1.8	5.6	..	..	1.9	..	..	..	1.2
Chronic appendicitis . . . .	..	..	..	11.1	1.3	1.4	..	..	1.0
Chronic bronchitis . . . . .	5.3	..	..	..	..	..	2.0	..	1.0
Eczema . . . . .	1.8	..	..	..	1.9	..	..	..	1.0
Pregnancy . . . . .	..	..	..	..	1.3	1.4	..	..	0.7
Toxic goitre . . . . .	..	..	..	..	1.9	..	..	..	0.7
Early nephritis . . . . .	..	..	..	..	0.6	1.4	..	4.8	0.7
Brachial neuritis . . . . .	1.8	..	..	..	1.3	..	..	..	0.7
Acne vulgaris . . . . .	1.8	..	..	..	0.6	..	2.0	..	0.7
Blepharitis . . . . .	1.8	..	..	..	0.6	..	..	..	0.5
Gastroduodenal ulcer . . . .	3.5	..	..	..	..	..	..	..	0.5
Bronchial asthma . . . . .	1.8	..	..	..	..	1.4	..	..	0.5
Cirrhosis of liver . . . . .	3.5	..	..	..	..	..	..	..	0.5
Sacro-iliac strain . . . . .	1.8	..	..	..	..	..	2.0	..	0.5
Urethral stricture . . . . .	3.5	..	..	..	..	..	..	..	0.5
Intestinal adhesions . . . .	..	..	..	..	0.6	..	..	..	0.2
Toxic arthritis . . . . .	..	..	..	..	..	1.4	..	..	0.2
Cholelithiasis . . . . .	..	..	..	..	0.6	..	..	..	0.2
Epididymitis . . . . .	1.8	..	..	..	..	..	..	..	0.2
Angina pectoris . . . . .	1.8	..	..	..	..	..	..	..	0.2
Frontal sinusitis . . . . .	..	..	..	..	0.6	..	..	..	0.2
Paresis of right external rectus	..	..	..	..	0.6	..	..	..	0.2
Trachoma . . . . .	..	5.6	..	..	..	..	..	..	0.2
Number . . . . .	57	18	14	9	157	73	51	21	400

Among the gastric neuroses we have grouped all those instances of gastric disturbance in which we did not believe that there was an organic lesion. In spite of the high percentage of such cases reported by others we found only 7 per cent. to be so affected, and none of these showed a marked disturbance. The diagnosis of gastroduodenal ulcer was twice made.

A secondary anemia was found ten times. The diagnosis was based upon the history, the physical appearance, and a study of blood smears. No hemoglobin estimations were made because of the difficulties of making accurate determinations under the circumstances of our work.

Backache was complained of by only 6 workers, of whom 4 were cigarmakers and 2 banders. Although many seemed to sit in strained positions there were backs to most of the seats, and this was doubtless a large factor in eliminating this complaint. In only 2 instances could a diagnosis of sacro-iliac strain be made.

Old inactive tuberculous lesions of the lungs were discovered 6 times, and active pulmonary tuberculosis was suspected in 5 of the 55 individuals in whom there were questionable physical signs of apical infiltration. In these 5 the physical signs alone were little more conclusive than in the others, and none had sputum, but some had a slight temperature elevation and all of the 5 were losing weight, were anemic, or had vague gastric disturbances. This small number of instances of tuberculosis agrees with Dembo's<sup>45</sup> finding of only 8 in her examination of 600 female tobacco workers, and with her cases gives a percentage of 1.3 for 1000 tobacco workers. In view of this small proportion of tuberculous pulmonary infections among these workers it is difficult to understand the high mortality rate of tobacco workers from this cause. It is possible of course that in some of those in whom we found vague signs at one or the other apex, and whom, because they were without symptoms of any kind, we have not included in this grouping, death may finally occur from tuberculosis. Another possibility is that working conditions have greatly improved in recent years, and that it was these conditions rather than the tobacco itself which caused the high tuberculosis mortality.

Attention is called to the 4 cases of eczema observed, in only two of which, however, was the lesion upon the hands. Knowles<sup>46</sup> has seen 9 instances of eczema upon the hands and fingers of tobacco workers and thinks it is probably due to the irritating effects of nicotine.

Although 7.6 per cent. of all the females showed some fulness of the thyroid gland, in only three of them could we elicit any signs of thyroid intoxication, and these were slight and questionable. Our diagnoses have been limited to these 3 cases, 0.7 per cent. of the total number and 1 per cent. of the women.

Brachial neuritis, although very mild in type, was diagnosed 3 times, and in each instance it was in a cigarmaker. Two cases of arm pains and one of leg pains in cigarmakers were recently reported by the State Board of Labor and Industries of Massachusetts,<sup>47</sup> and Dr. David Edsall informs the writer that he has seen a number of other cases at his clinic in Boston. Inasmuch as all our cases and some of the others occurred in a single process it is probable that the neuritis is mechanical rather than toxic in origin.

In only 12.2 per cent. of the workers were we unable to find any defects or symptoms, and for these we have entered diagnoses of "apparently normal," recognizing that it is impossible to say with certainty what is normal.

CONCLUSIONS. 1. The literature upon the effects of working in tobacco favors the view that it predisposes the worker to pulmonary tuberculosis, gastro-intestinal disturbances, anemia, genital abnormalities, and nervous conditions.

2. In a study of the social and medical conditions of 400 cigar workers in Philadelphia we did not find support for any of these contentions.

3. We did find, however, some wearing of the teeth and some pharyngeal and conjunctival congestion, findings which we believe to be dependent upon faulty personal and factory hygiene.

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## ELECTROCARDIOGRAPHIC OBSERVATIONS IN TOXIC GOITRE.

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THE importance of cardiac signs and symptoms in exophthalmic goitre has been a matter of common knowledge since the earliest description of this disease by Parry<sup>1</sup> in 1786. Tachycardia, palpitation, forcible heart action, and less often cardiac arrhythmia are such important factors in the syndrome that Möbius<sup>2</sup> was led to the dictum that "Basedow patients suffer and die through their hearts." It is only within the past decade or so, however, that the cardiac symptoms have been generally considered as due to thyrotoxic influences, rather than wholly or in part due to embarrassment of the right heart following an often hypothetical pressure on the trachea by the enlarged thyroid gland. As this condition constitutes a relatively simple example of an endogenous intoxication, it has seemed advisable to study the changes produced in the electrocardiogram by the intoxication of this disease, with the additional hope that further light might be thrown both on the resulting cardiac condition and on the changes produced in it by surgical operations on the thyroid.

**METHOD.** To this end electrocardiograms were taken on 51 goitre patients seeking surgical relief, in as many cases as possible both before and at short and long periods after operation. Information was sought not only as to the rate and rhythm of the heart action in both simple and toxic goitre cases, but also as to the relative size of the chambers of the heart and to other changes in the form of the ventricular complexes of the electrocardiogram

both before and after operation. Endeavor was also made to correlate these findings with the changes observed in the clinical condition of the various subjects examined. On account of the nervous state of many of the patients, fine vibrations of the string were often unavoidable, and occasionally were sufficient to prevent accurate measurement of the *P-R* interval, but did not otherwise interfere with interpretation of records. A still greater handicap was imposed by ineradicable extraneous electrical disturbances which, together with the limitations of the Edelmann galvanometer, prevented the proper complete standardization of records. For this reason it has been impossible to base any deductions on the actual changes in the size of the ventricular complexes observed in a given case after thyroid removal, and only the relative shapes of the various complexes in the pre- and postoperative records could be considered. Time intervals, the diagnosis of existing arrhythmias, and the detection of right or left ventricular preponderance were, of course, not interfered with. Most of the cases here reported were from the clinic of Dr. C. H. Frazier, whom I take this opportunity to thank for placing them at my disposal.

**RESULTS.** *Clinical.* The clinical data on the cases studied will be included in a table to be published later.

The usual preponderance of females, the relative youth of most of the cases, and the presence of the characteristic symptoms of the disease are all apparent. It is also obvious that almost all cases were of the toxic, hyperthyroid, or exophthalmic goitre type, and that this diagnosis was confirmed by pathological examination. Thirty-five of the patients submitted to partial thyroidectomy, 10 to artery ligation, and 2 to enucleation of adenomata. Of the ligation group 1 was greatly improved, 5 moderately so, 3 showed little or no improvement, and 1 died. In general this group did not tend to show as marked improvement as did those who had a partial excision. Although 3 of the latter failed to show any improvement after operation, it must also be remembered that many of the partial excision group had previously had arteries ligated, without sufficient improvement to obviate further surgical intervention.

Of the 47 cases, 7 were greatly improved by the operation, 23 were moderately improved, 14 only slightly or not at all improved, and 3 died. One of the deaths (Case No. 22) occurred two days after double lobectomy of a colloid goitre and was due to pneumonia complicated by increased thyrotoxicosis; another (Case No. 40) was due to cardiac failure twenty-four hours after ligation of a single artery. It is unfortunately true that in neither case were adequate premonitory signs evident either in the clinical examination or the electrocardiograms taken a few days before operation. The third case (Case No. 13), which had failed to improve after ligation of the superior thyroid artery, developed

negative *T* waves which were still present at the time of the second operation four months later. Her death from cardiac failure two

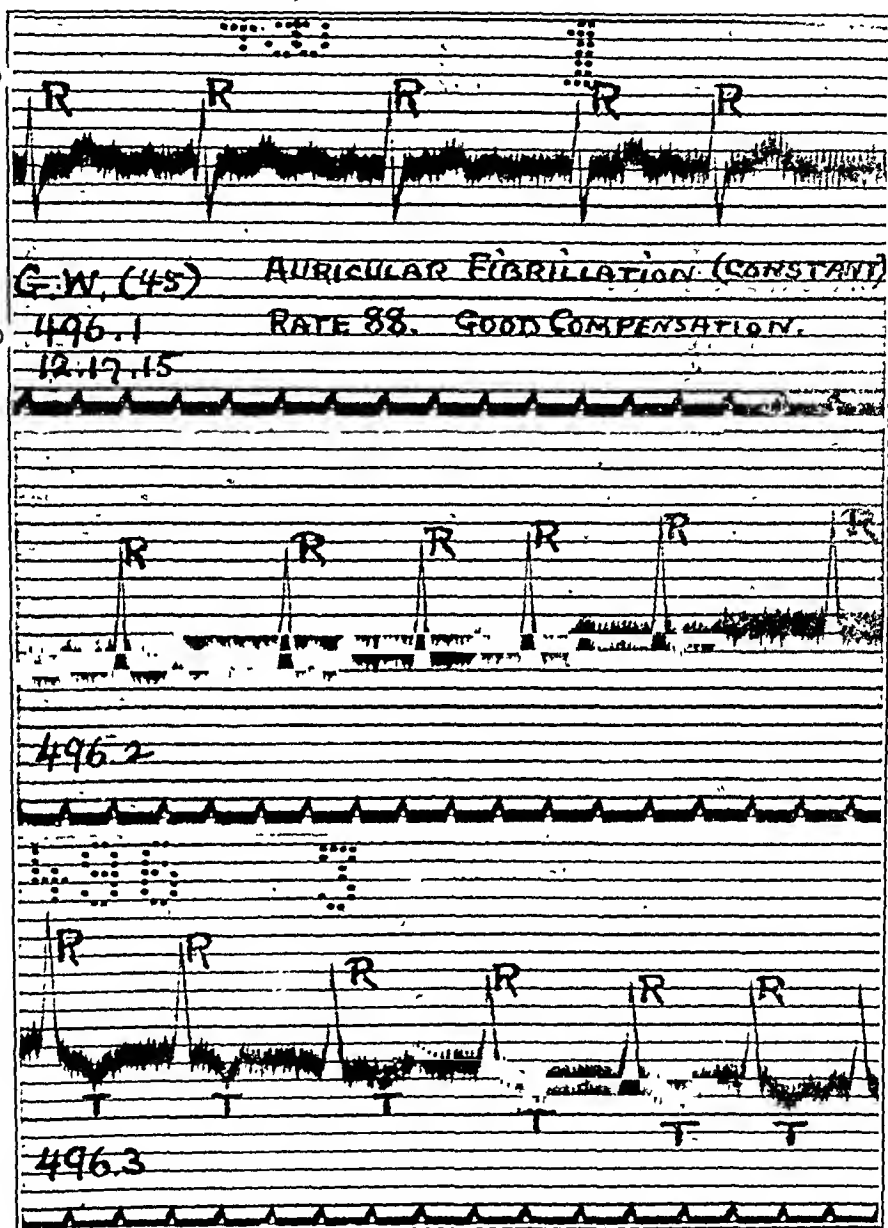


FIG. 1.—Case 45. Electrocardiogram of G. W., showing permanent auricular fibrillation. This and subsequent electrocardiograms were made with the Edelmann galvanometer. As the string could not be standardized with the patient in circuit, 1400 ohms were added as an arbitrary equivalent of the patient's resistance. Platinum strings were used with a resistance varying between 3500 and 5000 ohms. Time intervals are expressed at the bottom of each lead by  $\frac{1}{3}$ -second intervals. In this figure note (1) absence of sign of auricular contraction (*P* wave); (2) ventricular arrhythmia (irregular occurrence of *R*); (3) occasional fine waves of fibrillation.

days after the partial excision undertaken at this time tends to confirm the view that negative *T* waves, when not due to digitalis



medication, have an unfavorable influence on prognosis. The electrocardiogram of the patient that died from pneumonia showed abnormal *T* waves in Leads II and III, but similar abnormalities were found in 4 other cases (Cases 2, 3, 5, 35) that were improved by operation.

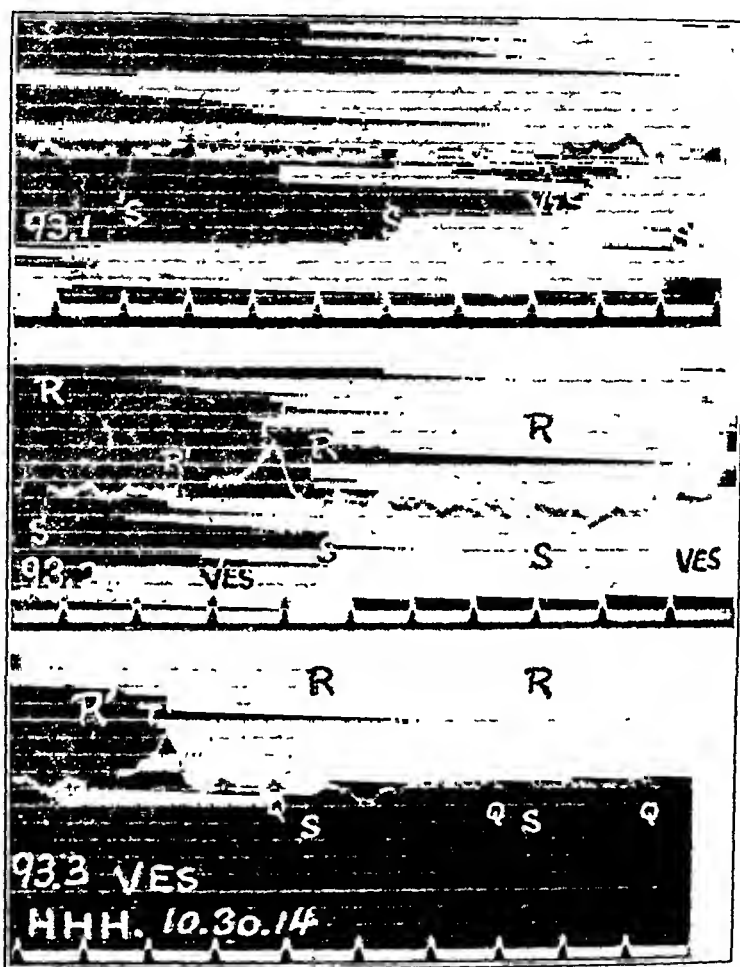


FIG. 2.—Case 24. Electrocardiogram of H. H. H., showing right ventricular preponderance, auricular fibrillation of probably ten years' duration, with occasional ventricular premature contractions arising from several sites. Note (1) that the *S* wave has replaced the *R* wave in Lead I and that the *R* wave of Lead III (*R*<sub>3</sub>) is greater than the *R* wave of Lead II (*R*<sub>2</sub>). Note also that (2) in each lead one or two complexes vary greatly from the normal supraventricular type, and that (3) the same disturbance of mechanism exists as in Fig. 1.

**RHYTHM.** Changes in cardiac rhythm were observed in 11 cases, as follows: sinus arrhythmia, 4 cases; ventricular extrasystoles, 3 cases; auricular fibrillation, 3 cases; auricular flutter, 1 case. The *P*-*R* interval was prolonged beyond normal limits in 2 cases. As no other adequate cause for such derangement of cardiac

mechananism was given in the past history of all but 2 of these cases, it is fair to assume that the majority, if not all, were caused by the thyreotoxicosis, acting not only by its direct toxic effect, but also indirectly through the cardiac hypertrophy and later degeneration

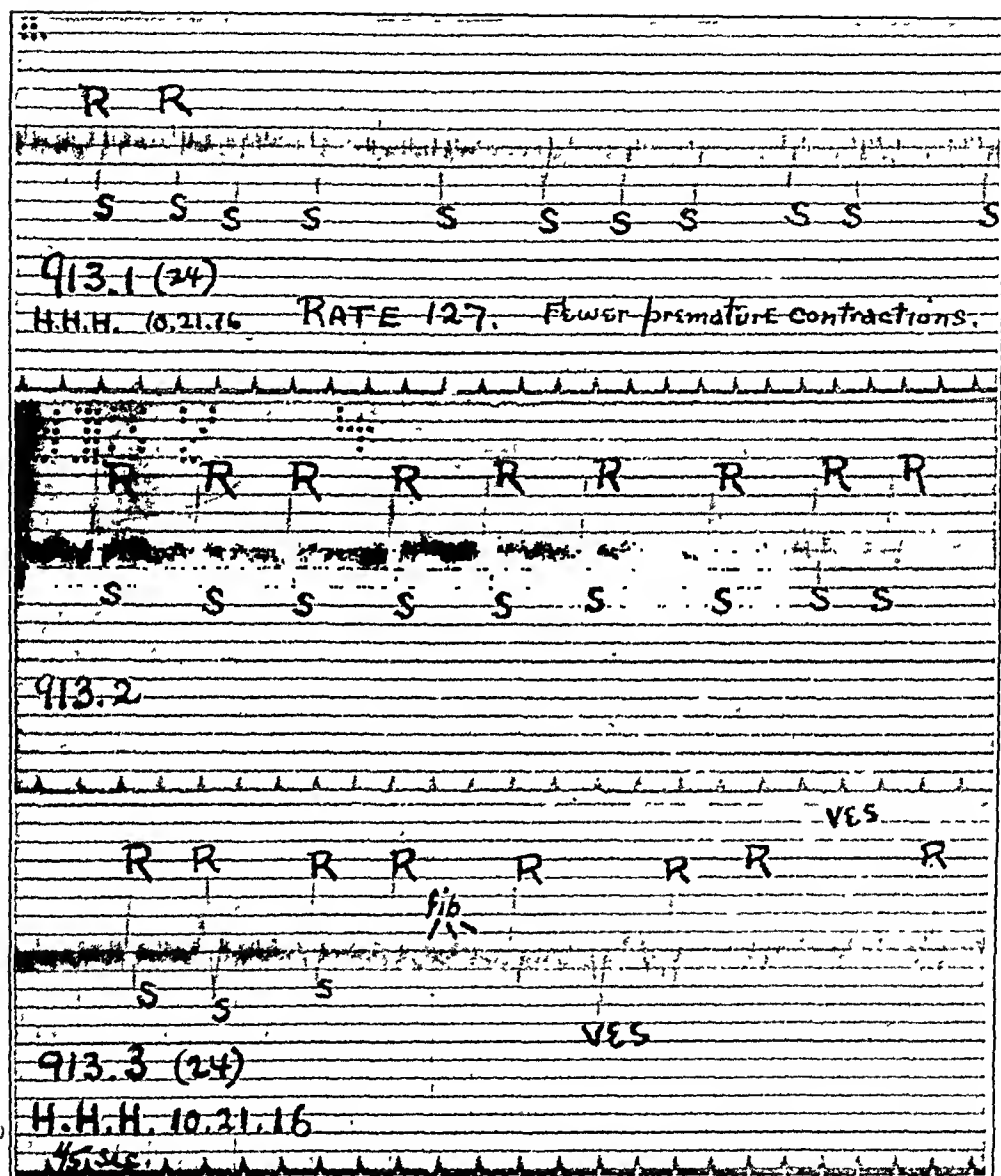


FIG. 3 —Electrocardiogram of same patient as Fig. 2, taken two years later, showing the same picture, except that the premature contractions occur much less frequently.

thus caused. The fact that most of the cases studied received energetic treatment relatively early in the disease will probably account for the comparative infrequency of the more important arrhythmias and of other gross cardiac changes in this series. This in its turn



The small number of arrhythmic cases affords but little opportunity to judge of the effects of operation on the arrhythmia. The case of flutter and two of the cases of fibrillation were undoubtedly permanent, having been followed over several years without change. Although many different attempts were made at different times to change the auricular flutter into fibrillation or normal rhythm all efforts proved unavailing. One of the cases of auricular fibrillation (Case 51) proved to belong to that interesting group of transient fibrillation, to which attention has elsewhere been called.<sup>3</sup> In Fahrenkamp's<sup>4</sup> series of cases of hyperthyroidism in which transient fibrillation was present the arrhythmia occurred in distinct paroxysms of short duration. In the present case, however, fibrillation was present when the patient was first seen eighteen months ago. On account of a coexisting mitral stenosis and the absence of data as to the time of origin of the arrhythmia it was thought at that time that an ordinary case of fibrillation with chronic mitral endocarditis was being complicated by hyperthyroidism. The fibrillation persisted apparently as a constant condition until about one month ago, when it was noted that coincident with general improvement the pulse had become regular. Electrocardiograms taken then and at various periods since then show that normal rhythm has now supervened. As this occurred coincident with improvement in the hyperthyroidism it is fair to assume that the thyroid and not the endocarditis was the chief factor in the production of the fibrillation.

Of the 3 cases exhibiting extrasystoles only 1 accepted surgical treatment, and in this case the extrasystoles disappeared after operation, just as frequently happens in this type of arrhythmia, when the source of toxemia is removed or diminished.

Although sinus arrhythmia is not usually considered to have any clinical importance, it was found to be lessened after operation, along with the signs of clinical improvement. Attention might here be called to the work of Thorne,<sup>5</sup> who considers that, like the other arrhythmias, though in a lesser degree, sinus arrhythmia is never found in a truly normal heart. Whether this belief is accepted or not, any procedure that tends to lessen an existing sinus arrhythmia should be considered a step in the direction of improving the cardiac condition.

#### EXPLANATION OF FIG. 4.

FIG. 4.—Case 26. Electrocardiogram of A. K., showing auricular flutter, with a varying degree of A. V. block, probably of four years' duration. In this as in the other electrocardiograms of this series records were taken from the three customary leads; the tension of the string was so standardized that 1 millivolt caused a deflection of 1 cm. Time intervals in this record are expressed by heavy and light vertical lines across each lead, representing  $\frac{2}{5}$  and  $\frac{1}{25}$  second respectively (Cambridge galvanometer). Each deflection is lettered according to Einthoven's scheme, and a diagram is added for each lead to illustrate the changing heart block. Note the prominent inverted (diphase) P waves in Leads II and III.

Two cases (Cases 4 and 8) showing distinct prolongation of the P-R interval in the absence of digitalis medication are the only

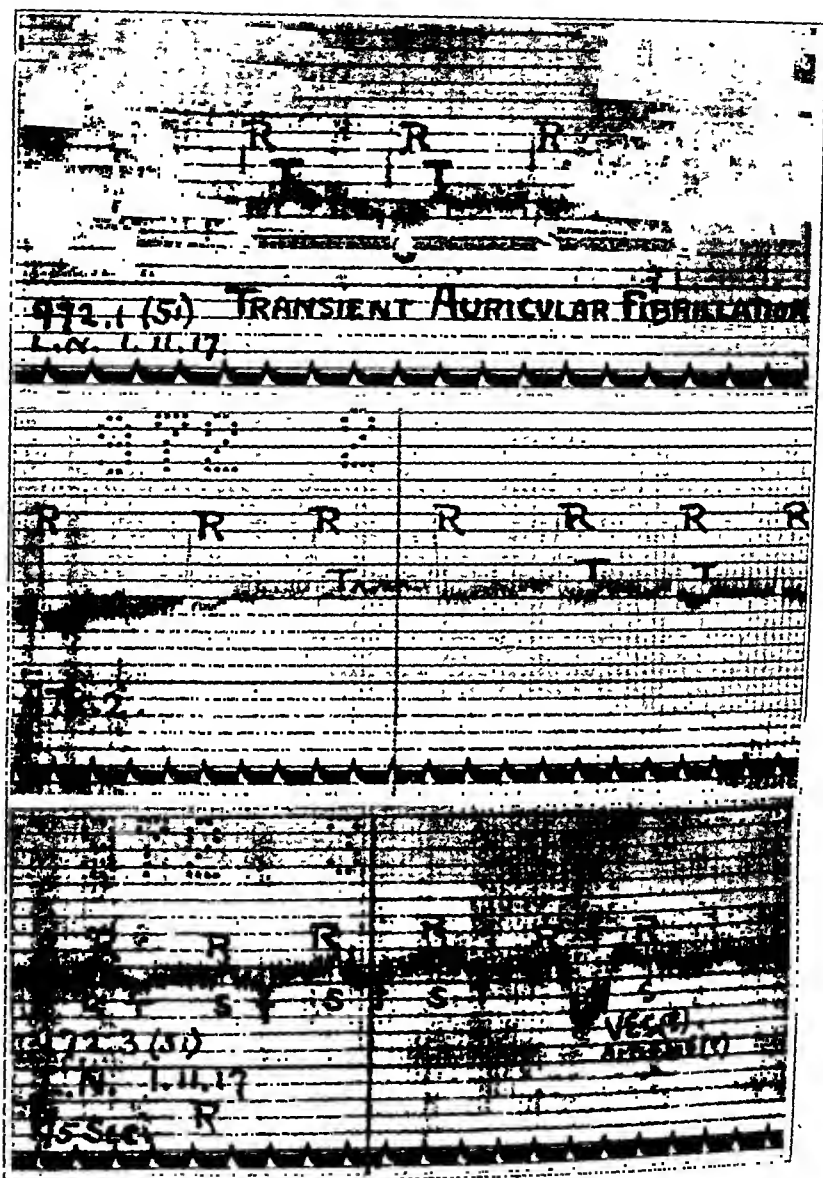


Fig. 5.—Case 51. Electrocardiograms of L. N., showing transient auricular fibrillation. Note that although the ventricular arrhythmia is slight, the same disturbance of mechanism exists as in Fig. 6.

examples of defective conductivity in this series. Reilingh,<sup>6</sup> however, has shown that more advanced degrees, even complete heart-block, may occur in exophthalmic goitre.

*Blood-pressure.* The systolic and diastolic blood pressure was estimated soon after admission to the hospital, and in many cases shortly before discharge. The most noteworthy abnormality was

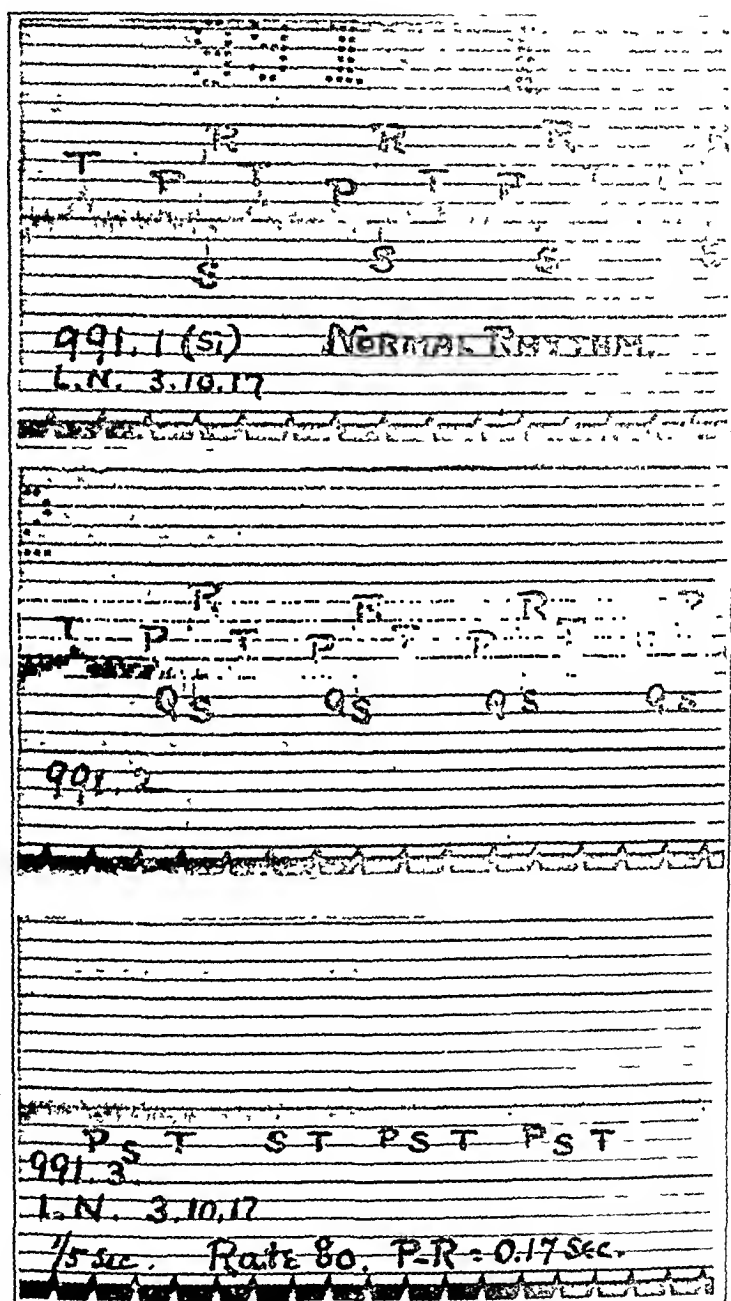


FIG. 6.—Electrocardiogram taken two months later, showing normal rhythm. Note (1) reappearance of P; (2) regular ventricular rhythm; (3) absence of irregular waves of fibrillation.

the increased pulse-pressure, which was over 60 mm. Hg in 11 patients who showed no signs of hypertension. The increase in pressure, which was due both to elevation of the systolic and

depression of the diastolic pressure, is in all probability to be explained as the vascular response to the overacting heart. In 5

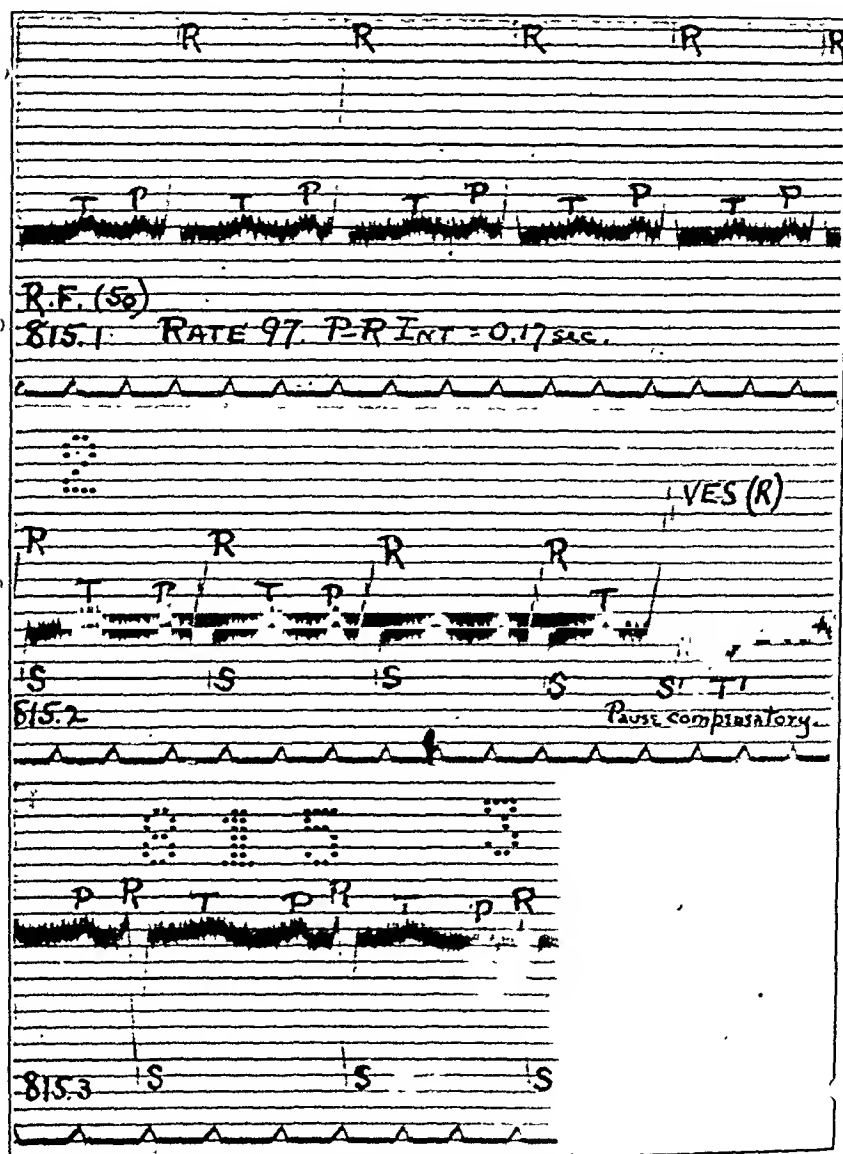


FIG. 7.—Case 50. Electrocardiogram of R. F., showing left ventricular preponderance and one ventricular premature contraction. Note that  $R_1$  is greater than  $R_2$  and that  $S_2$  is greater than  $R_3$ . In Lead II note that the last ventricular complex varies greatly from the other complexes of the lead and occurs prematurely (extrasystole).

cases the systolic pressure was above normal limits, but in only 1 were signs of hypertensive nephritis or arteriosclerosis present. In at least 1 case the pressure fell to normal as the patient improved,

so that this, too, should be considered a sign of cardiac intoxication. The 3 cases that showed a lowered systolic pressure (below 110) are difficult to explain, but it should be noted in all of these that a

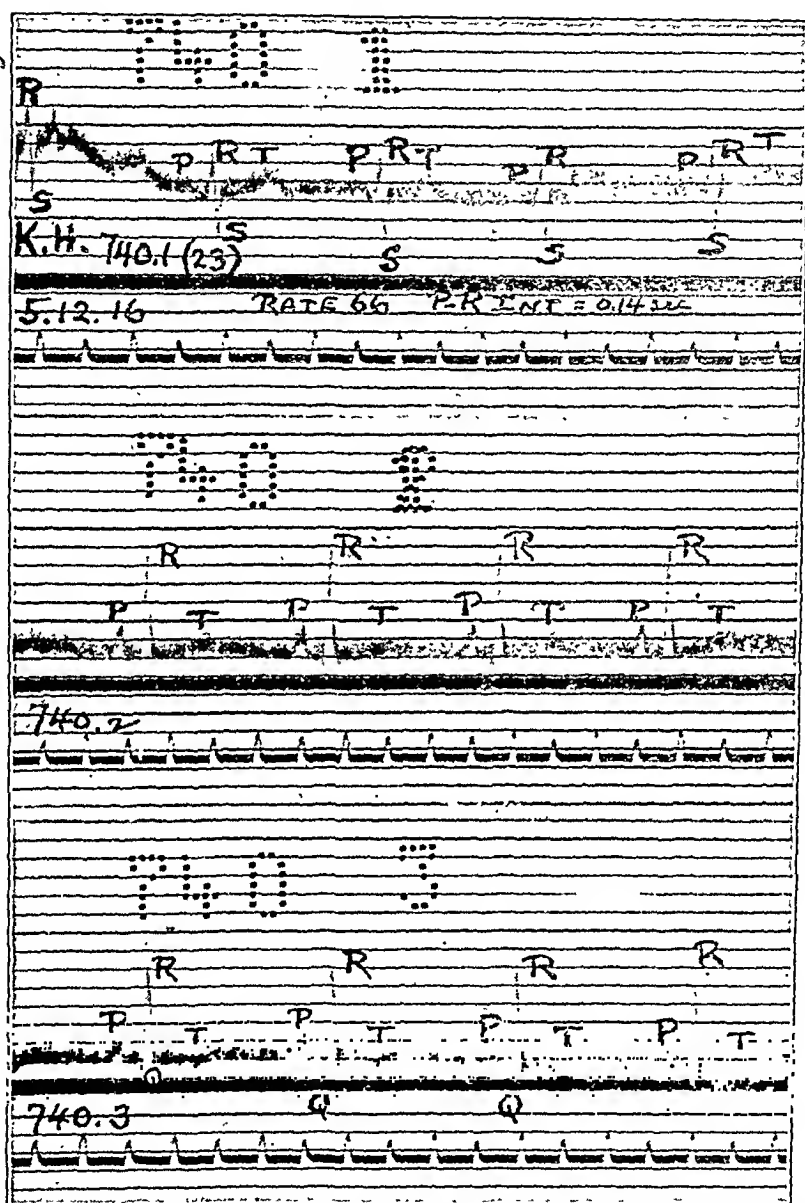


FIG. 8.—Case 23. Electrocardiograms of K. H., showing lessened degree of right ventricular preponderance after operation. Note that whereas  $S_1$  is greater than  $R_1$  in the first record, it is distinctly less in the second. Also  $R_3$ , instead of being the same size as  $R_2$ , is less than  $R_2$  in the second record.

normal pulse-pressure was preserved. Although due to a different kind of disturbance these changes, as has been pointed out by Taussig,<sup>7</sup> are of the same kind as those found in aortic regurgitation, and may be considered as characteristic of toxic goitre.



*Changes in Form of the Ventricular Complex.* From the point of view of the cardiographer, one of the items of this study that was approached with the liveliest anticipation was the question as to what effect the thyreotoxicosis and also its treatment by surgical operation would have upon the cardiac function as expressed by

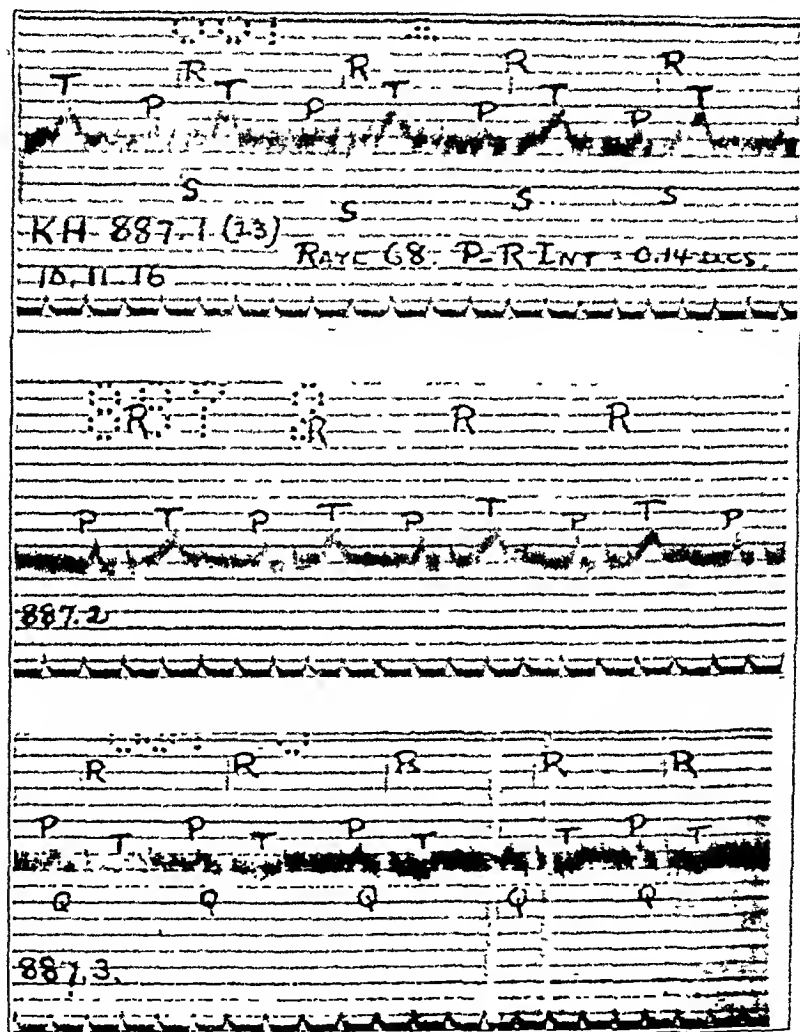


FIG. 9.—Same case as Fig. 8.

the form of the ventricular complex. As an analyzer of cardiac arrhythmias the string galvanometer has already been thoroughly and satisfactorily exploited. As a gauge of the functional capacity of the heart, however, in demonstrating abnormalities in form of the ventricular complex, its possibilities are still far from being realized. Lewis<sup>5</sup> has called attention to the fact that "if in any

subject electrocardiograms which show considerable divergence from what is regarded as normal are obtained it is probable that the heart is abnormal." This has corresponded to our experience

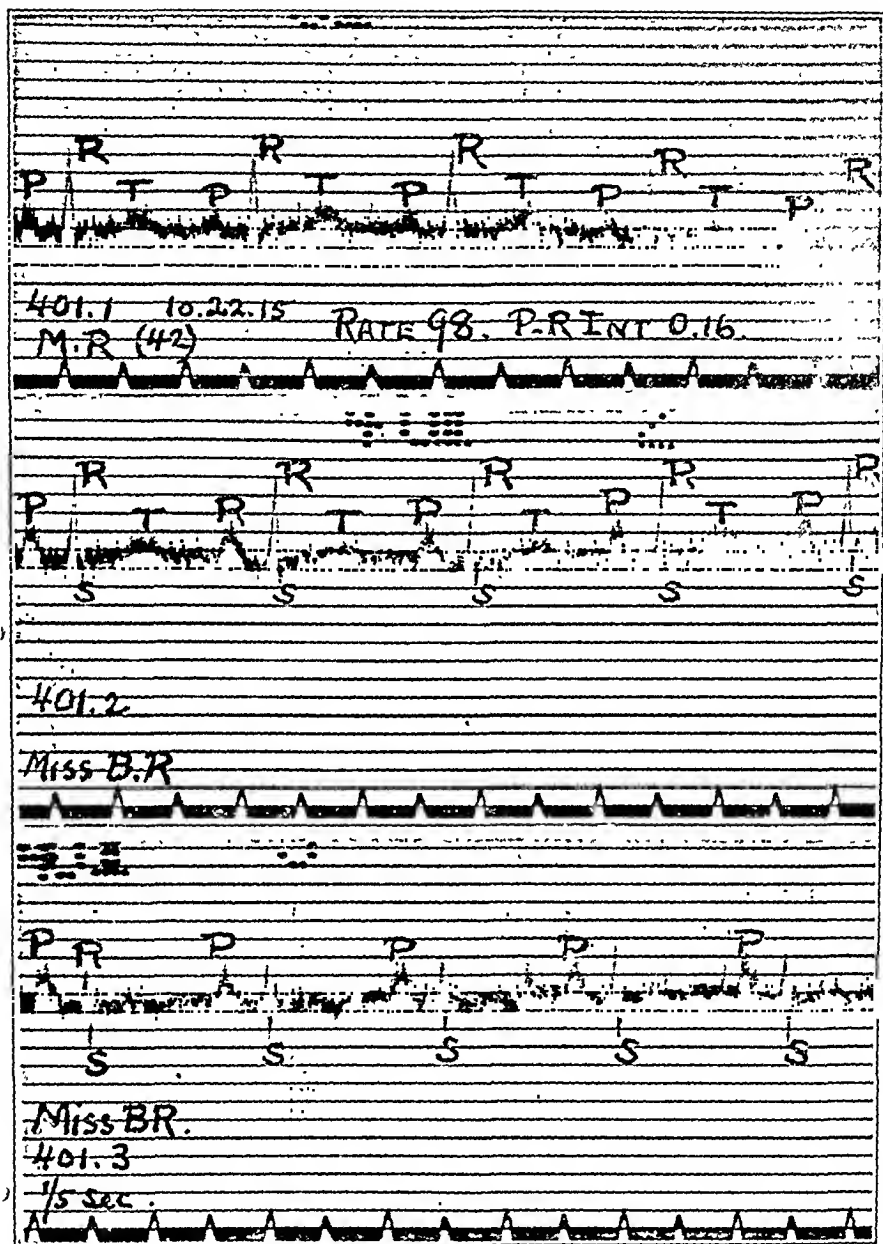


FIG. 10.—Case 42. Electrocardiograms of M. R. before and after operation, showing lessened *T* wave after operation and a more marked degree of left ventricular preponderance. In the second record note that the *T* waves are less than in the first (especially in Lead I); also that *R*<sub>1</sub> has become slightly longer than *R*<sub>2</sub> and that *S*<sub>3</sub> is proportionately longer than *R*<sub>3</sub>. (See Fig. 11.)

in this clinic, although we cannot subscribe to "the converse proposition that if the summits fall within the normal limits of amplitude the heart is probably normal." We have seen in 2 cases

of this series, as well as in several other cardiac cases examined electrocardiographically, that the electrocardiogram was well within normal limits shortly before death from cardiac failure, and that even the form of the complex might be nearer normal shortly before

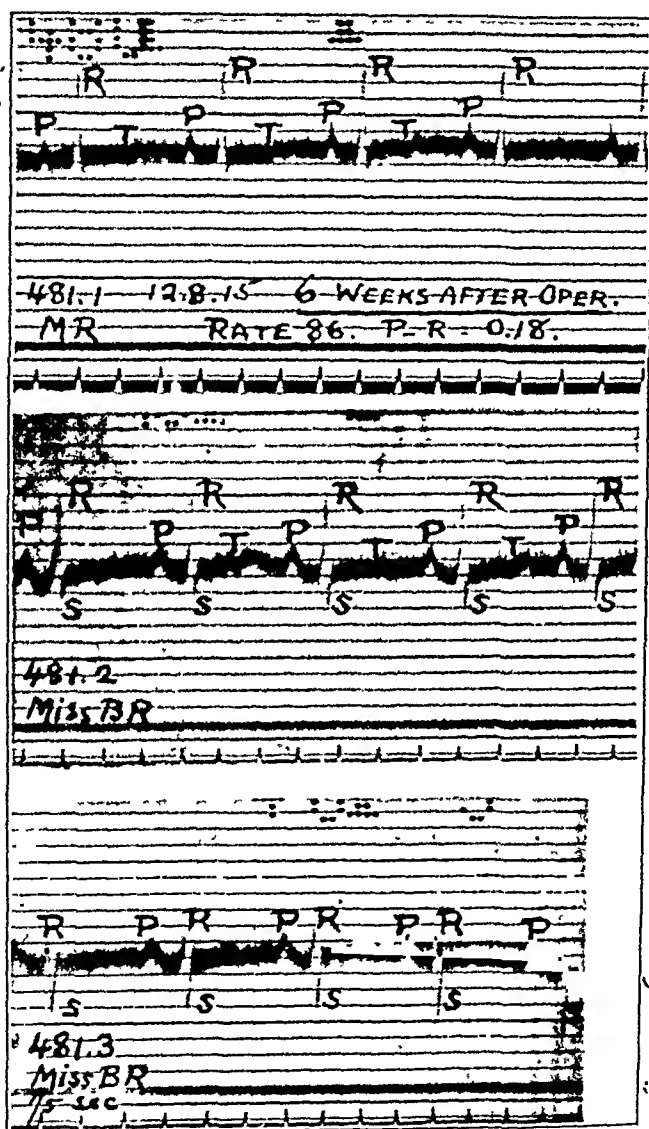


FIG. 11.—Same case as Fig. 10.

or during acute cardiac failure than it had been when the patient was clinically in better condition.

Preoperative variations from the normal form of the ventricular

complex not only include such changes as those showing hypertrophy of one or other ventricle but also notchings and



various changes in form of the *T* wave. Essentially normal electrocardiograms in both form and rhythm were found in 22 of the 51 cases of the series.

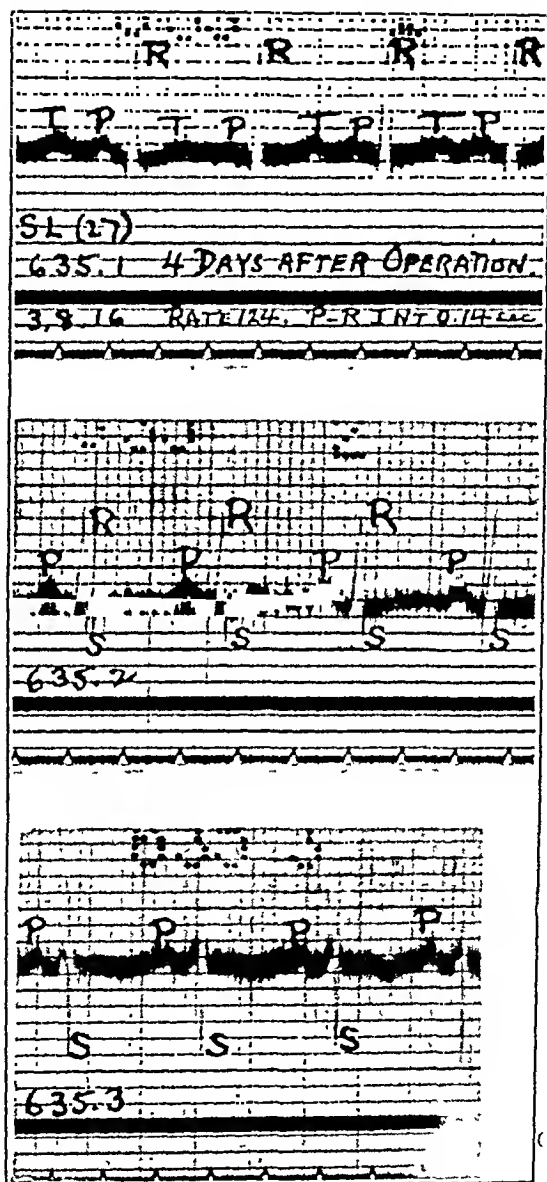


FIG. 13.—Same case as Fig. 12.

*Hypertrophy of Auricles and Ventricles.* Although the electrocardiogram registers action currents whose intensity depends on the strength of stimulus production, certain characteristic changes in the form of the ventricular complex have been recognized as indicat-

ing a preponderating hypertrophy of one or other ventricle. The evidence as to hypertrophy that is obtained in this way is more accurate and reliable than either the results of percussion or orthodiagraphic examination. The deduction as to the size of the muscle mass is nearly always true, because the stimulus going to

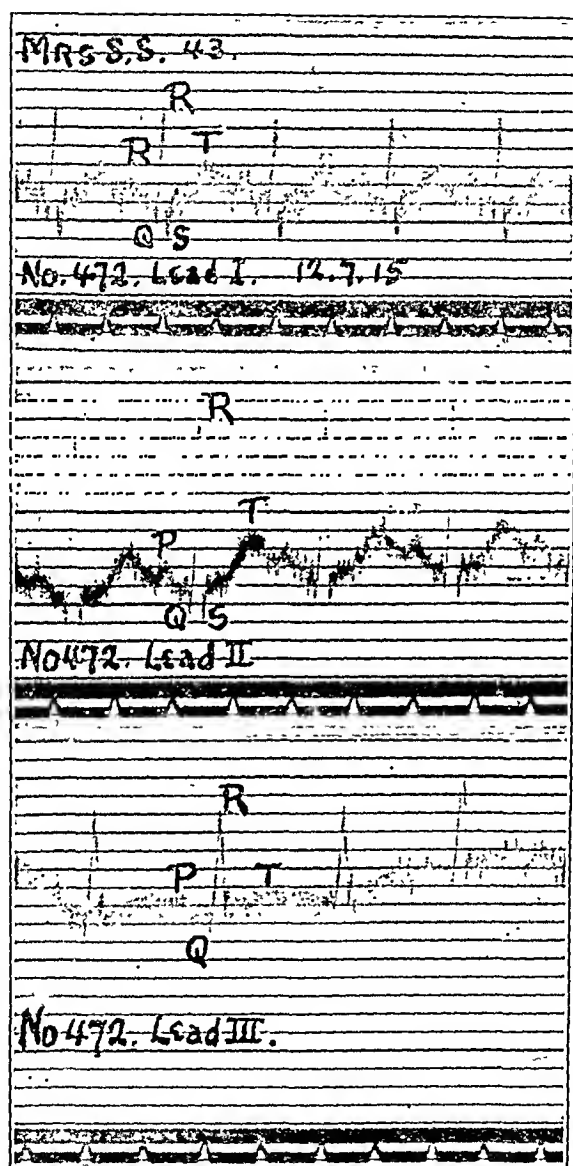


FIG. 14.—Case 43. Electrocardiograms of S. S., showing lessened *T* wave after operation that persisted for at least six months after operation.

the hypertrophied muscle mass is nearly always correspondingly increased. Some of the cases of this series, however, and also experimental work still in progress, indicate that the form of the ventricular complex (*i. e.*, the intensity of the stimulus production) may be noticeably changed without the occurrence of equivalent

change in muscle mass. Alterations occur within a few days after operation, when it would have been impossible for the muscle mass to have changed materially. The change in form that follows change in the axis of the heart has been shown to be relatively slight and clinically negligible, and is therefore not considered in this series.

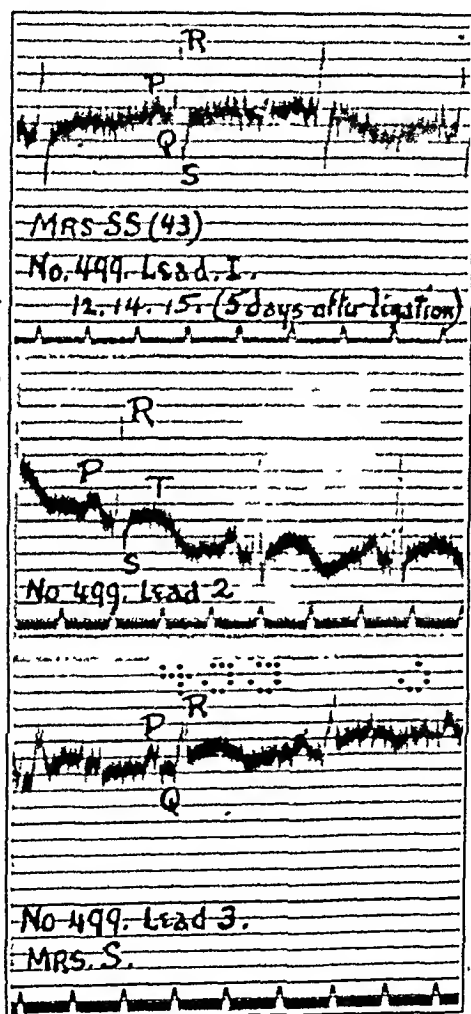


FIG. 15.—Same case as Fig. 14.

The state of right ventricular preponderance (R. V. H.) has been considered as present when both the  $S$  wave of Lead I ( $S_1$ ) is greater than the  $R$  wave of Lead I ( $R_1$ ) and when  $R_3$  is greater than  $R_2$  and when  $Q_2$  and  $Q_3$  are unusually large. When one of these factors is present or when the waves in question approach equality the condition is spoken of as a "tendency to R. V. H." Similarly

when  $R_1$  is greater than  $R_2$  and  $S_3$  greater than  $R_3$  and  $Q_1$  prominent the state of left ventricular preponderance is recognized, and when this condition is approximated it is spoken of as a "tendency to left ventricular preponderance."

In the present series the majority of cases betrayed no signs of ventricular hypertrophy in the electrocardiogram. This is in accord with the experiences of other writers. Contrary to the general

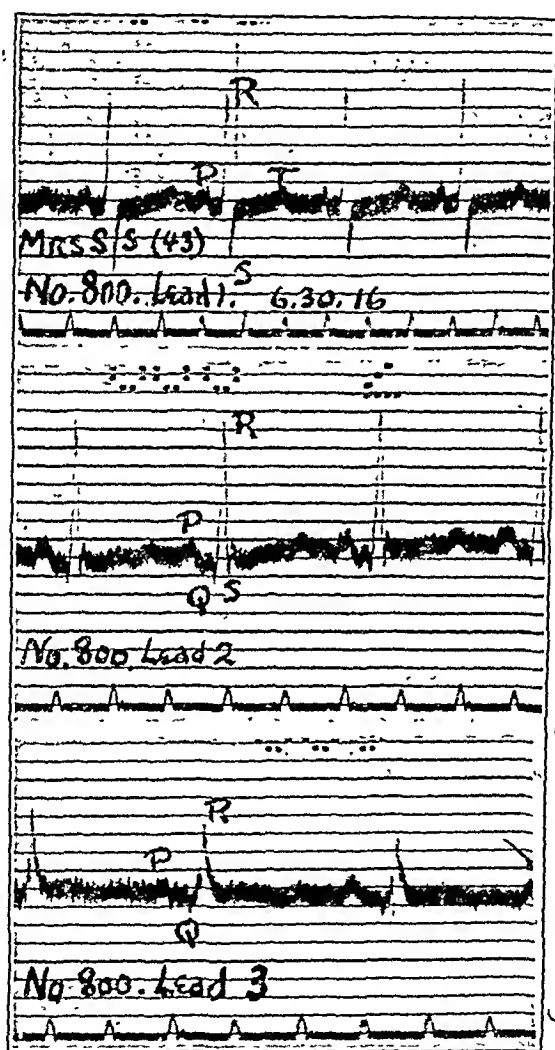


FIG. 16.—Same case as Fig. 14.

opinion, however, when hypertrophy was present, right ventricular preponderance has proved to be as common as left. It was distinct in 3 cases and a tendency to it existed in 8 cases. Left ventricular preponderance occurred in 6 cases and a tendency to it in 5 cases. It is difficult to explain why some cases of uncomplicated toxic goitre should develop right and others left ventricular preponderance. The most probable explanation would be that the left pre-



ponderance is due to whatever causes are responsible for the increased systolic pressure; whereas in the right preponderance cases other factors, such as relatively or actually incompetent mitral valve, would be considered as playing a more important

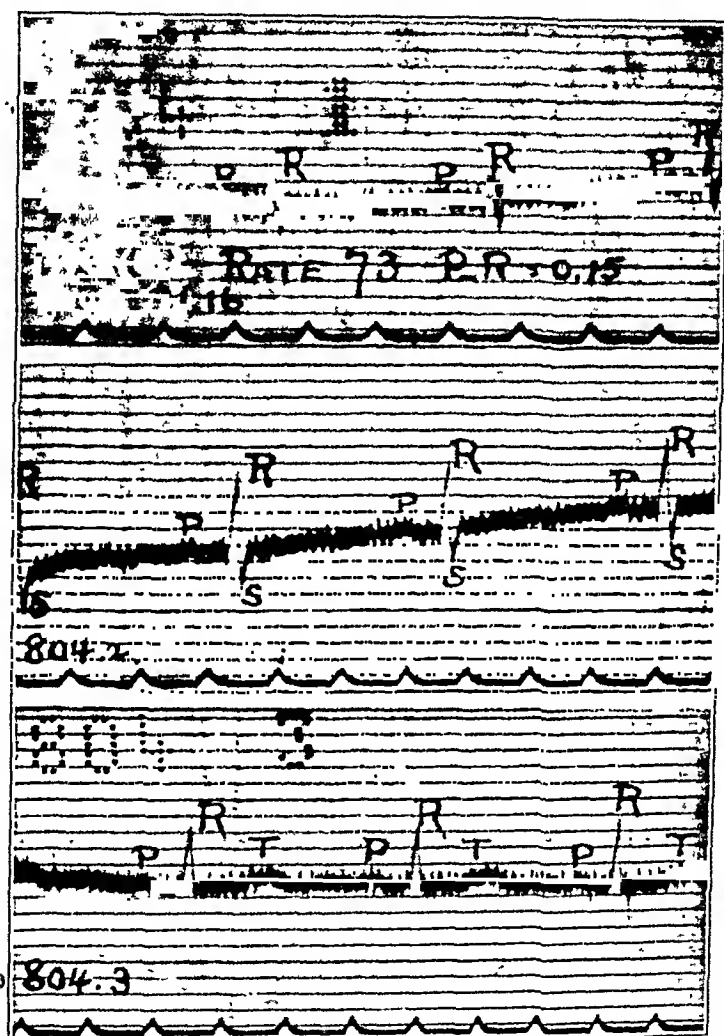


FIG. 17.—Case 13. Electrocardiograms of M. C., showing development of a negative *T* wave after operation. That this may be considered as a bad prognostic indication is supported by the death of this patient from cardiac failure after a second operation.

part. Some significance may be attached to the fact that the average duration of the disease in the right ventricular cases was under two and a half years, whereas in the left ventricular cases it was over four and a half years.

After surgical operation 5 of the right ventricle cases showed

less preponderance, 3 showed no appreciable change, and 2 an increased amount. Of the L. V. H. cases after operation, on the other hand, 4 showed no change, 6 showed an increased amount,

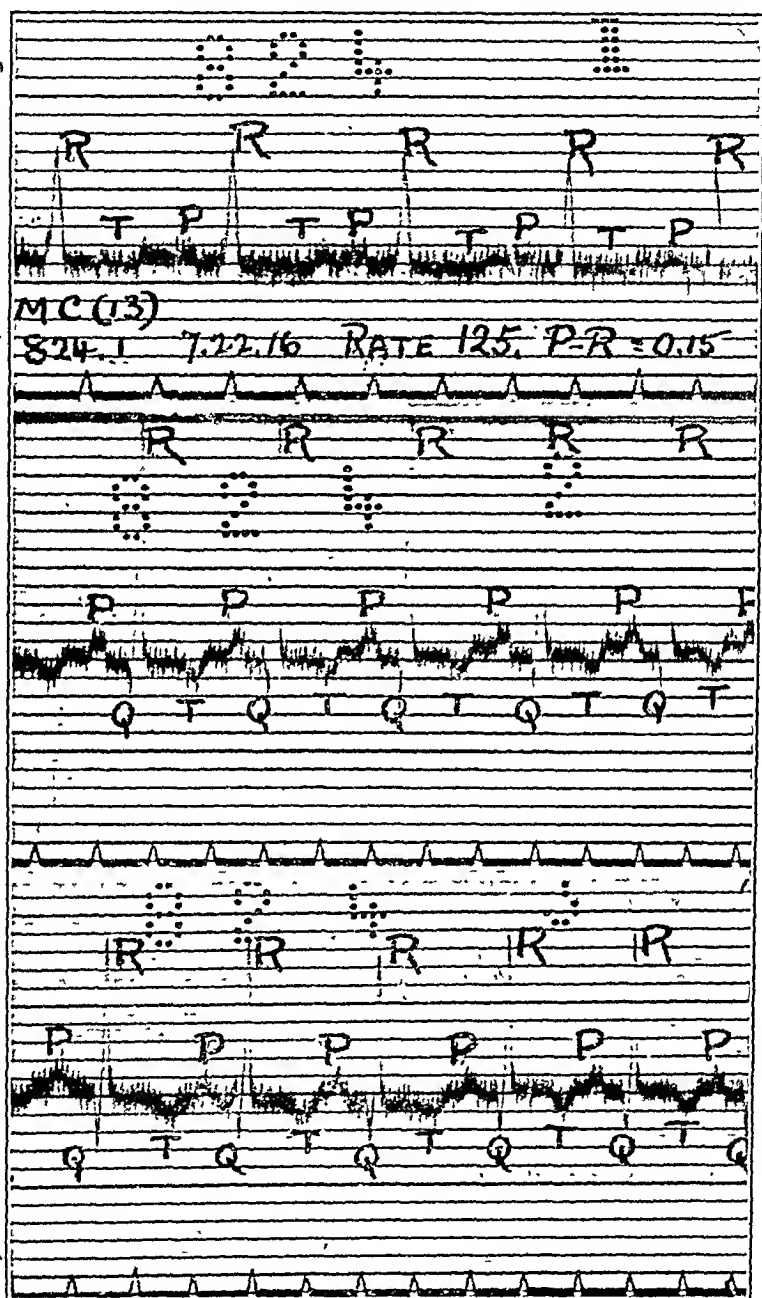


FIG. 18.—Same case as Fig. 17.

and only 1 showed a lessened degree of preponderance. This probably indicates that the left ventricular cases are due to a muscular hypertrophy that has already been accomplished and cannot be relieved by treatment even though signs of improvement are present.

The same reasoning may be applied to those right ventricular cases that do not change or progress. For those that showed lessened

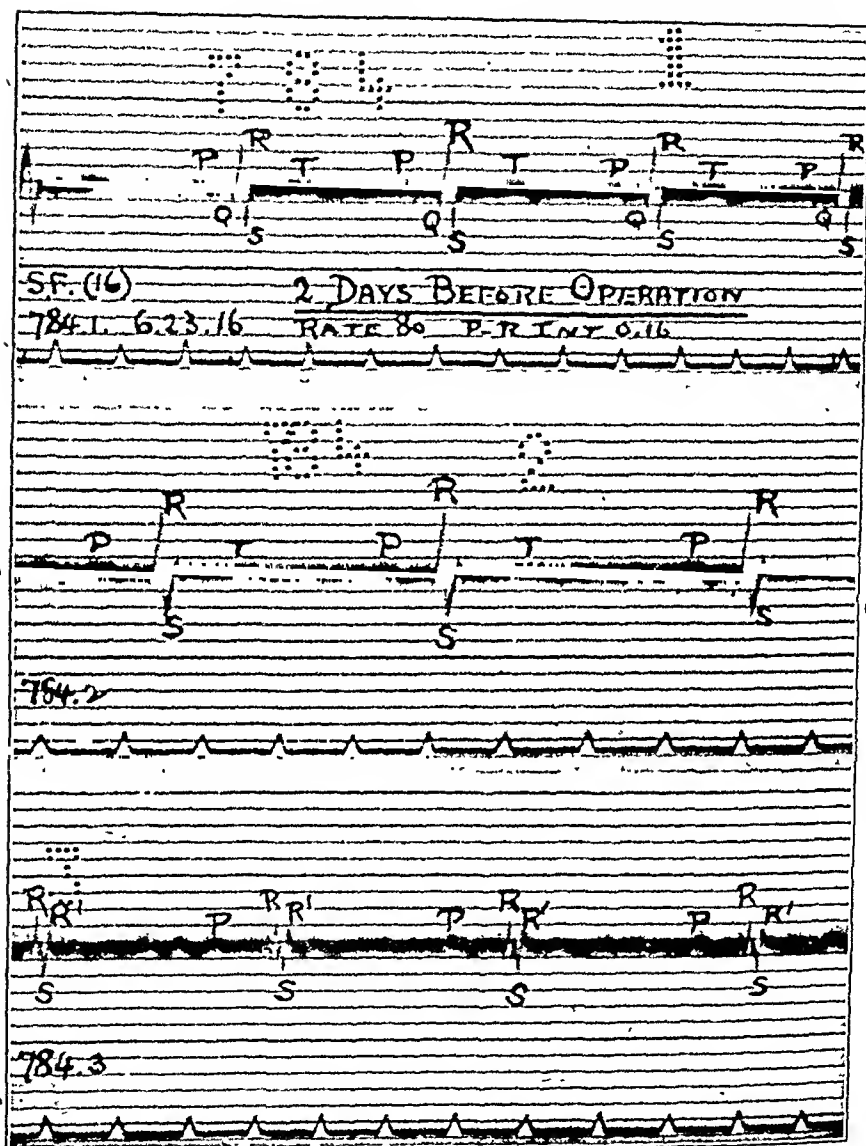


FIG. 19.—Case 16. Electrocardiograms of S. F., taken two days before, three days after, and twelve days after surgical operation, showing approximation of  $R_2$  to normal in the last records. Note that the deep notch of  $R_2$  in the first records becomes less and less noticeable in the second and third records. In this case the small postoperative  $T$  wave had already become larger by the twelfth day.

hypertrophy after operation a lessened impulse due to diminution of the intoxication might be assumed or possibly a nearer approach to competency of the mitral valve.

*Changes in T Wave.* In most of the cases of this series the *T* wave was well developed. This was especially noted in the more toxic cases and was even true in the 5 cases in which  $T_2$  was either diphasic or inverted and in both cases in which  $T_1$  was diphasic or

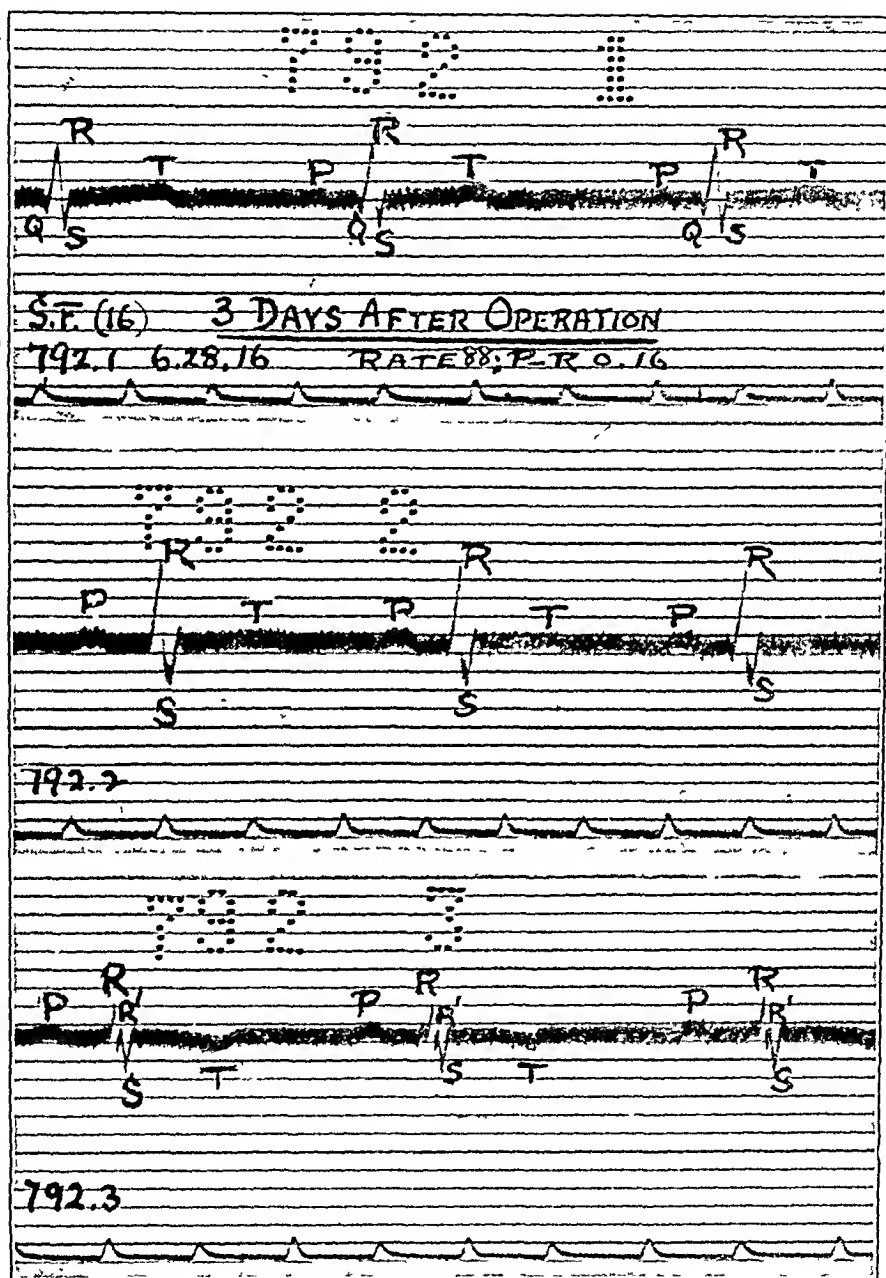


FIG. 20.—Same case as Fig. 19.

inverted. If in the absence of digitalis medication the *T* wave may be considered, as many authorities believe, as an index of the force of the cardiac contraction, such a result would be expected from the overacting goitre heart.

It is significant that out of the 23 cases that were examined within ten days of operation 11 showed a distinctly lessened *T* wave in all leads, coincident with general clinical improvement. One case also that improved greatly without operation exhibited

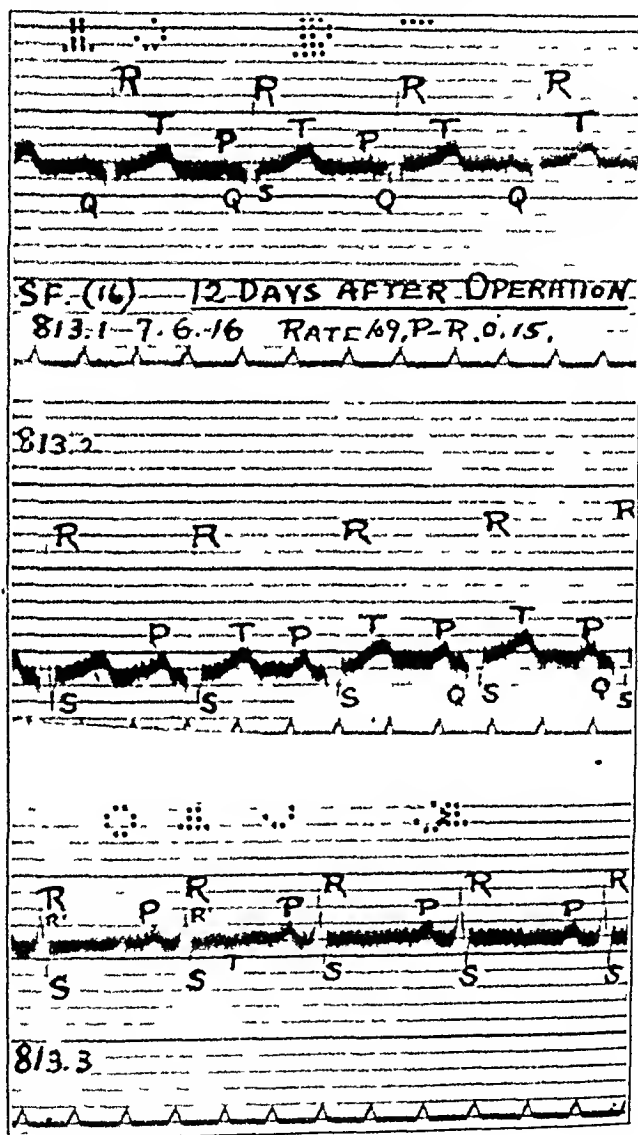


FIG. 21.—Same case as Fig. 19.

a diminished *T* wave in all leads during the improved period. The welcome deduction that could be drawn from these facts, to wit, that the smaller postoperative *T* wave indicated a quieting down of the overactive heart, was unfortunately complicated by

another observation, namely, that three control studies of three normal hearts showed the same tendency to a postoperative diminution of the *T* wave. This is a detail that in itself needs further

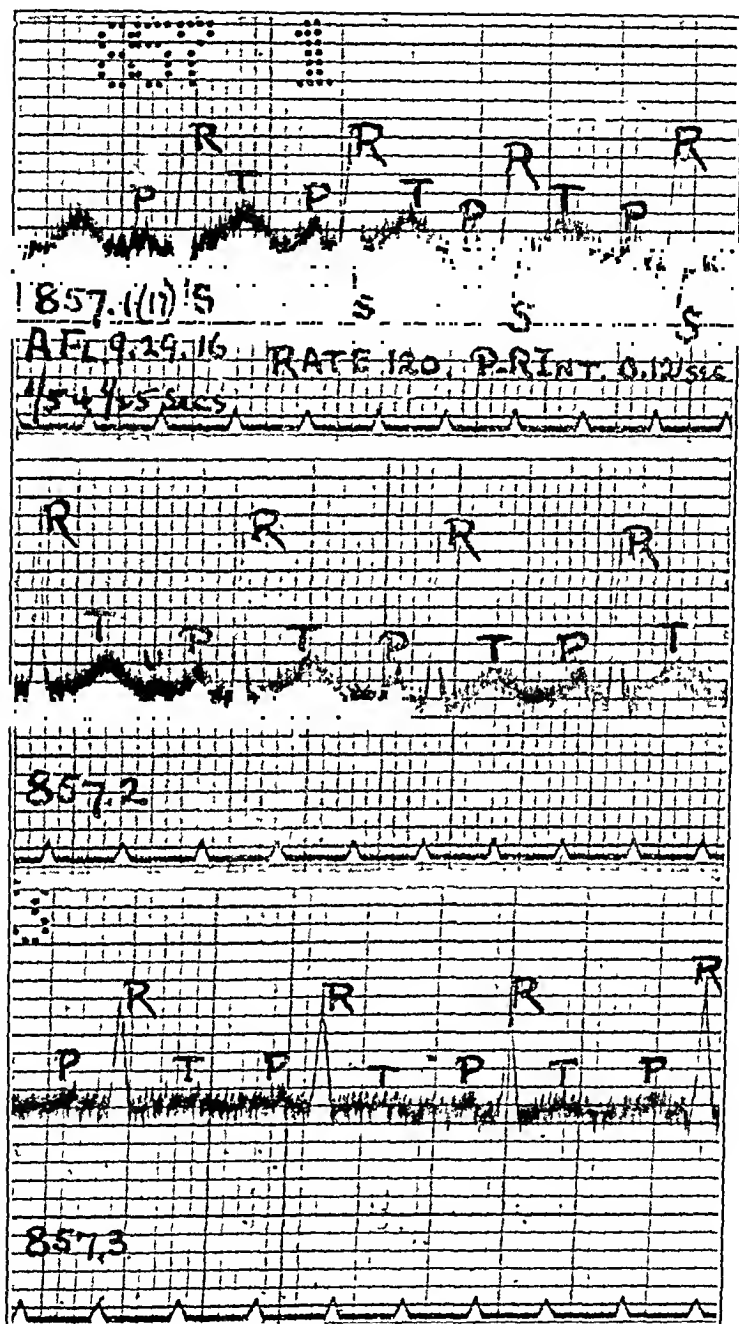


FIG. 22

investigation; at present, however, we are limited to the statement that such diminution is less in the normal than in the goitre cases and only lasts a few days. The diminution of the *T* wave of the

goitre heart is so much more accentuated and durable, often lasting three or more months, that it may be taken as highly probable that the heart's overaction has really been lessened and the treat-

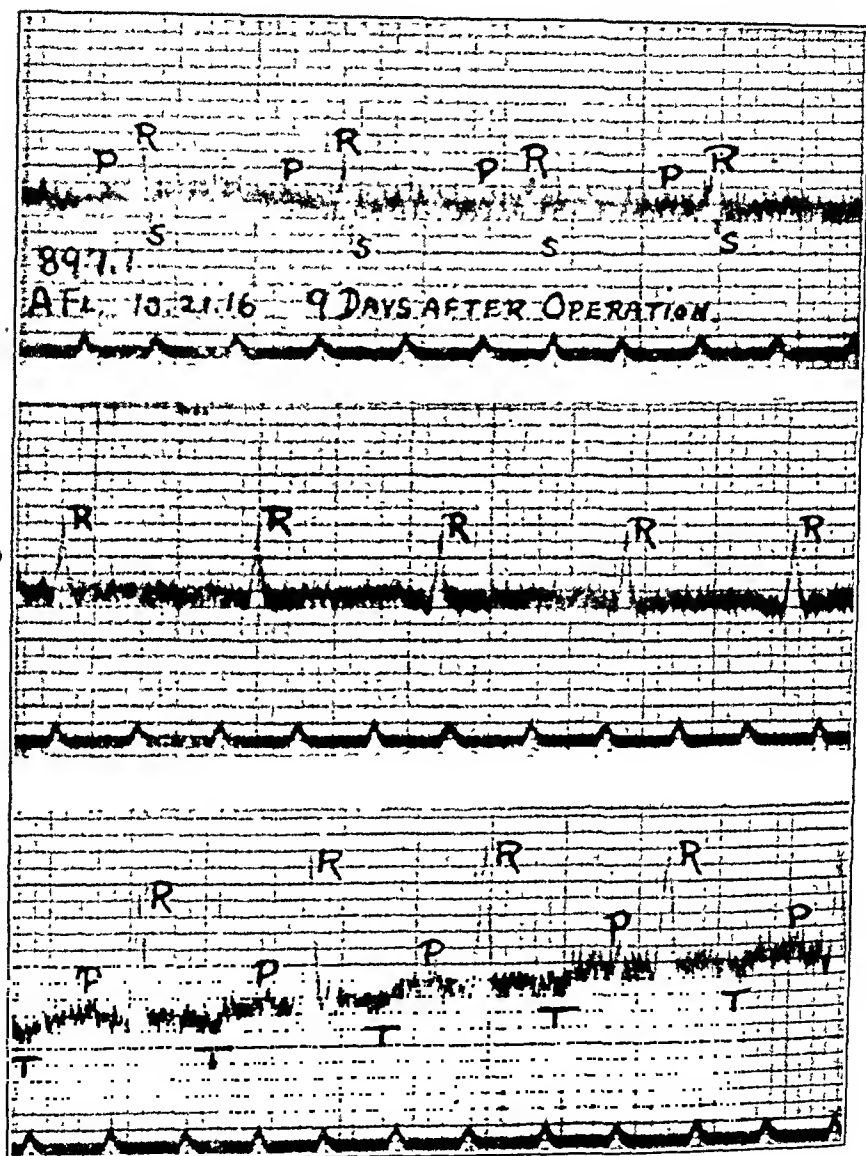


FIG. 23

ment been proved beneficial in so far as the electrical changes may be taken as a guide.

The persistent postoperative inversion of the *T* waves in one case (Case 13), with a subsequent fatal outcome to a second opera-

tion, has already been commented upon. In another case (Case 6) a failure to improve after operation was accompanied by the development of a negative  $T$  wave. In 2 other cases (Cases 28 and 51)

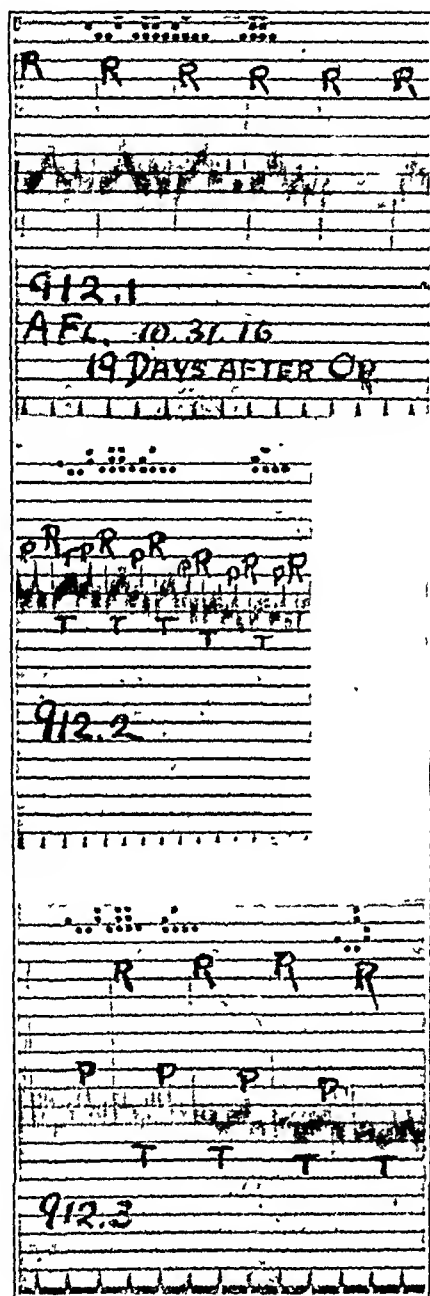


FIG. 24

general improvement during observation was accompanied by a change from negative to positive  $T$  waves. To this extent support is given to the idea that inverted  $T$  waves are of bad prognostic significance.



*Other Changes in Form of the Ventricular Complex.* In the form of the preoperative electrocardiograms various small changes from the established normal have been observed such as would be found in any similar series of cardiac cases. I refer to such details as unusually deep *S* waves in one or more leads, notching of the *R* wave and so forth. These were frequently changed after operation, or appeared after operation when they had previously been absent. As the significances of such changes, however, is not yet understood, and as they were often contradictory, no deductions can be drawn from them. Thus in Case 1 the *S* wave of an otherwise normal record was decreased in all leads after operation, whereas in Case 2 the *S* waves were all increased after operation. Case 16 (Fig. 11) presents an item of interest. In the preoperative electrocardiogram the *Q*, *R*, *S* group of Lead III was a bizarre collection of three upward and two downward peaks. Three days after operation, while the patient's general condition was improving, Lead III showed these peaks in such modified form that they could be explained as a deep notching of an *R*, *S* group. Nine days later, coincident with further improvement, Lead III had almost approached a normal complex, the notch being higher on the *R* wave and barely visible. While such anomalies are common in Lead III, and while their underlying cause is unknown, nevertheless it is reasonable to assume that the nearer approach of the electrocardiogram to a normal form is indication of an improvement in the cardiac mechanism.

**SUMMARY.** 1. Electrocardiographic studies have been made of 51 cases of goitre, mostly of the toxic type, in as many cases as possible both before and after surgical operation.

2. In the series of 47 patients that submitted to surgical operation (ligation, partial excision, and enucleation of adenomata) 3 deaths occurred; 2 of these offered no premortuary signs in either clinical or electrocardiographic examination; in the third case the development of negative *T* waves might have served as an adequate warning.

3. Electrocardiograms, essentially normal as to form and rhythm, were found in 22 cases (43 per cent.). Preponderating hypertrophy of the right ventricle (or a tendency thereto) was found in 11 cases, and of the left ventricle (or a tendency thereto) also in 11 cases. After operation, however, one-half of the right ventricular cases showed a diminished degree of preponderance, whereas all but one of the left ventricular cases showed either no change or an increased amount of preponderance.

4. Cardiac arrhythmia was found as follows: sinus arrhythmia, 4 cases; ventricular extrasystoles, 3 cases; auricular fibrillation, 3 cases; auricular flutter, 1 case; delayed conductivity, 2 cases. Two of the cases of fibrillation and the case of flutter proved constant over several years. The other case of fibrillation was of the

transient kind and disappeared coincident with the improvement that followed medical treatment.

5. The *T* wave was found to be unusually prominent in most cases. In about half the cases it was markedly and persistently diminished after operation. This was found to be true to a lesser degree in postoperative cases with normal hearts. Other changes in form of the ventricular complex after operation indicated an approximation to normal cardiac mechanism.

6. Blood-pressure estimation showed an increased pulse-pressure in most cases that was diminished with the improvement that followed surgical relief. Systolic pressure was also high in those cases that showed left ventricular preponderance, but never exceeded 170 mm. Hg.

CONCLUSIONS. 1. In early cases of toxic goitre the characteristic tachycardia is not accompanied by any signs of myocardial change that are demonstrable with the string galvanometer.

2. With persisting overaction of the heart, hypertrophy of either ventricle may become manifest.

3. Progressive hypertrophy and overaction results in myocardial degeneration that may be manifested by any type of cardiac irregularity: sinus arrhythmia, premature contractions, auricular flutter, auricular fibrillation, heart-block, etc.

4. If the existing intoxication is the chief factor in the production of the arrhythmia this may disappear with removal of the intoxication.

5. Successful treatment, whether medical or surgical, improves the cardiac condition by this means. This is shown not only by the occasional disappearance of an arrhythmia but also by diminution in the size of the *T* wave and in the pulse-pressure as well as by the general clinical condition.

6. The development of diphasic or inverted *T* waves, especially in Leads I and II, should probably be considered as influencing prognosis unfavorably.

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# ROENTGENOLOGICAL STUDIES IN THE HEALING OF GASTRIC AND DUODENAL ULCERS.<sup>1</sup>

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It is a common experience that the interpretation of cure of chronic gastric ulcer is difficult because of the spontaneous remissions and exacerbations of symptoms so frequent in the clinical history of these patients. The need of more definite and objective evidence of cure has been apparent for some time. In the attempt to secure such evidence we have been interested during the past two years in studying these patients by means of repeated roentgenological examinations before, during, and following medical treatment. Our method is as follows:

1. In addition to the regular routine of history-taking, physical examination, test-meal examination, etc., the patient is subjected to a thorough preliminary roentgenological study, including the registering of from six to twelve plates, taken at intervals after the barium meal.

2. In the event that positive roentgenographic evidence of ulcer is thus obtained, the patient is put under medical treatment (the details of which do not concern us here) for from three to six weeks. Within this time and before discharge from the hospital the patient is again thoroughly studied roentgenologically, including the making of plates.

3. The patient is asked to report back to the hospital at least every three months for a repetition of the roentgenographic studies.

In other words, roentgenological examinations are made before, during, and after medical treatment, as often as every three months, for a period of one to two years or longer. These studies serve as a guide to the healing process, and as a contrast with the findings before treatment was begun.

Thus far we have studied in this fashion 11 cases, of which 7 are lesser curvature cases and 4 are duodenal.

In this paper I shall refer very briefly to the results of this study.

I. LESSER CURVATURE ULCER. Haudek,<sup>2</sup> in 1910, described his classical *Nischen Symptom*, which was the demonstration roentgenologically of a small round projection (*Ründliche Vorsprung*) along the lesser curvature of the stomach. Haudek believed that this projection or pocket represented the accumulation of

<sup>1</sup> Read at the Twentieth Annual Meeting of the American Gastro-Enterological Association, Atlantic City, 1917.

<sup>2</sup> Die Roentgendiagnose des Kallösen Magengeschwürs und ihre Bedeutung, Münch. med. Wehnschr., 1910, S. 2463.

bismuth or barium in the crater of a penetrating ulcer. In certain cases the pocket or crater of bismuth was surmounted by a small air bubble which could be observed in the plate.

Haudek's observations and conclusions have been confirmed by many workers both in this country and abroad. During the course of our work we have had abundant opportunity to examine such stomachs either at the operating table or at autopsy, and have likewise been assured of the correctness of Haudek's work.

Cole,<sup>3</sup> in 1915, amplified Haudek's work, reporting a series of indurated gastric ulcers of the lesser curvature—with or without the niche—detected at a far earlier stage. Cole's method, which he describes, is that of serial roentgenography. Many of our plates, particularly those taken after medical treatment, strikingly resemble those of Cole's indurated ulcers.

Faulhaber,<sup>4</sup> in 1912, emphasized the importance of the spastic hour-glass stomach, either in conjunction with the Haudek niche or alone, as evidence of callous ulcer. While undoubtedly such hour-glass contraction occurs, in our experience they have been quite uncommon, while the lesser curvature projection has been quite frequent. In one case with a very pronounced hour-glass and a lesser curvature niche the operation failed to reveal an ulcer. This case will be referred to later in the discussion of the dangers of misinterpretation in this method of examination.

The positive identification of the niche to be in fact the ulcer crater may be seen in Figs. 1, 2 and 3 from Cases I, II and III.

The abstract of the history of the patient from whom Fig. 1 was taken is as follows:

CASE I.—L. S., blacksmith, aged fifty-seven years, Michael Reese Hospital.

*Complaint.* Pain in upper abdomen, loss of weight, recurring attacks every three or four months for the past two years. Pain sticking in character, one to two hours after meals. Two months ago had three attacks of hematemesis.

*Physical Examination.* Slight loss of weight, tender point in mid-epigastrium, otherwise negative.

*Test-meal Examination.* Continuous secretion, yeast cells, sarcinæ, normal acidity.

*Roentgenographic Findings.* "Lesser curvature contains a defect about two inches from the pylorus resembling that of a perforated ulcer." (Fig. 1.) Marked gastric retention after six hours.

*Operation.* Dr. L. A. Greensfelder: "On the posterior wall at the lesser curvature an easily palpable callous ulcer is found, approxi-

<sup>3</sup> Roentgen Diagnosis of Indurated Gastric Ulcer, Am. Jour. Roentgenology, November, 1915.

<sup>4</sup> Roentgendiagnostik der Magenkrankheiten, von Dr. M. Faulhaber, Sammlung Zwangloser Abhandlungen aus dem Gebiete der Verdauungs und Stoffwechsel Krankheiten, 1912, Band iv, Heft 1.

mately 4 cm. from the pyloric sphincter (Fig. 1). The thickened callous area was about 5 cm. in diameter and practically round. Pylorotomy, including resection of the ulcer, was performed."

In passing it is interesting to note that the location of the ulcer and its size corresponds very closely with the findings as obtained roentgenologically.



FIG. 1.—Case I. L. S. Lesser curvature ulcer. Roentgenogram and ulcer after excision.

The history of the patient from whom Fig. 2 was taken is as follows:

CASE II.—P. O., patient of the County Hospital, with a typical recurring history of gastric ulcer for eight years.

*Roentgenological Examination.* "Marked penetrating ulcer, lesser curvature half-way between the cardia and the pylorus." (Fig. 2.)

*Operation.* Dr. Paul Oliver: "Deep callous ulcer found on the lesser curvature in median portion of stomach. Ulcer resected. Gastro-enterostomy performed." (Fig. 2.)

Here also the close similarity between the roentgen-ray findings and the ulcer may be noted.



FIG. 2.—Case II. P. O. Lesser curvature ulcer. Roentgenogram, "niche," and ulcer after excision.

Fig. 3 is taken from the following case:

CASE III.—J. R., car repairer, aged fifty-four years. Cook County Hospital.

*Present Complaint.* Began fourteen months ago, consisting of epigastric pain one and a half hours after eating, with nausea and vomiting.

*Roentgen Ray.* "A rather large, penetrating ulcer is seen on the lesser curvature of the stomach." (Fig. 3.)

*Operation.* Dr. Paul Oliver: "Indurated ulcer on lesser curvature about 5 em. in diameter; some sear on serous surface with firm fibrous adhesions to the left lobe of the liver. Adhesions separated. Ulcer inverted by Lembert linen stitch. Posterior gastric jejunostomy."

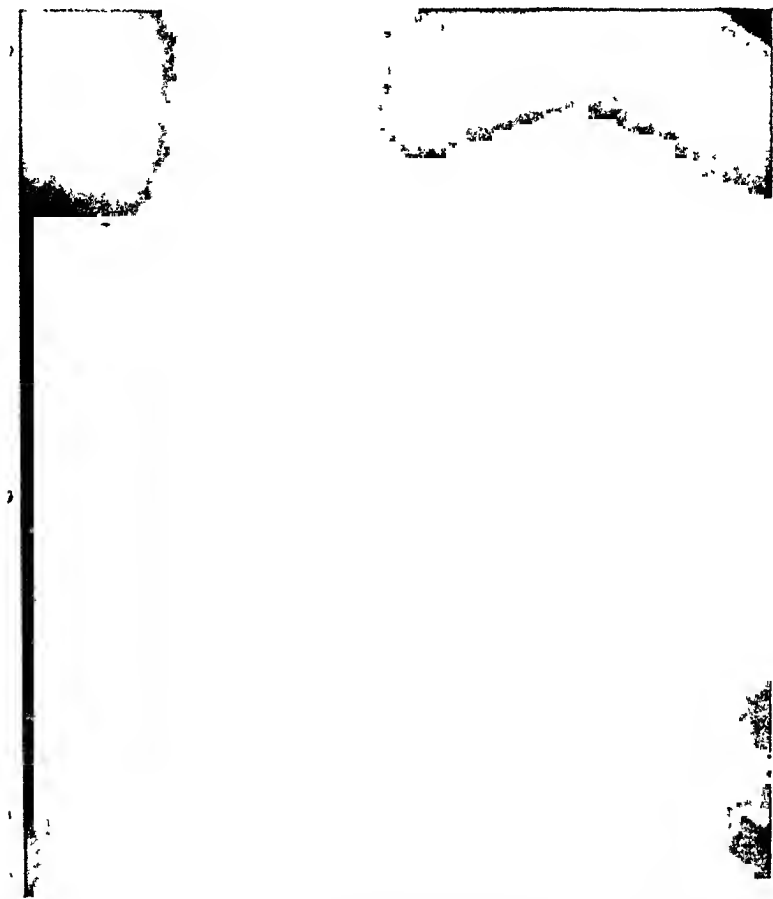


FIG. 3.—Case III. J. R. Penetrating ulcer of lesser curvature adherent to under surface of liver.

While the ulcer itself was not resected, and therefore could not be studied histologically, still the location and the findings agreed so exactly with the roentgen-ray picture that there can be no doubt regarding the identification of the projection with the adherent callous ulcer.

These three representative cases I believe are convincing proof of Haudek's contention that the niche does in fact represent the crater of a callous ulcer. That these ulcers were in fact callous gastric ulcers and not carcinoma was proved by serial microscopic section, in none of which was any evidence of malignancy noted.

The permanent cure of the first two patients following operative removal of their ulcer, the first for nine months and the second for three years, is substantiating clinical proof of the non-malignant character of their disease.

Accepting, then, as definitely established, that the barium projection represents the ulcer crater, let us turn to a consideration of the changes in morphology of the niche during and after medical treatment. In certain cases the depth and width of the projection gradually lessens until, in the favorable cases, it has entirely disappeared, leaving a smooth, regular, lesser curvature outline. This disappearance of the niche can be followed accurately from week to week and month to month, and is usually accompanied with coincident improvement in the clinical findings, viz., disappearance of epigastric pain and distress; cessation of vomiting; disappearance of occult blood in stool and stomach contents; gain in weight, appetite, hemoglobin, and general well-being of the patient; gradual return to normal of gastric secretion and motility. Such ulcers may be said to be *healing*, and in the event that these objective and subjective changes continue satisfactorily, may, at the end of six to twenty-four months, be said to be *cured*, depending on the personal conservatism of the observer.

Certain other cases, however, do not progress so satisfactorily, either because of insufficient dietary care on the part of the patient, inaccuracy in the details or duration of medical management, or because of other underlying organic disease, such as carcinoma, syphilis, and tuberculosis. In these ulcers the niche narrows only temporarily, later resuming its former contour or even becoming deeper, wider, and more irregular. Such patients demand either more accurate medical management, specific tuberculous or luetic treatment, or *surgery*—or all three.

The following 3 cases have been chosen as representative of the changes in the niche before, during, and after medical treatment.

CASE IV.—L. B.<sup>5</sup> male, aged fifty-four years.

*Complaint.* Patient has suffered from "indigestion" for twelve to fifteen years, consisting of periodical exacerbations of severe colicky pain. At different times diagnosis of chronic gall-bladder and appendix have been made.

*Radiographic examination* revealed a broad, deep, penetrating ulcer of the lesser curvature, midway between the cardia and the pylorus (Fig. 4).

After two weeks of medical treatment a second roentgen ray was made, showing marked diminution in the depth and width of the lesser curvature pocket (Fig. 5). This coincided with parallel clinical improvements.

<sup>5</sup> History and permission to report this case was kindly given by Dr. Jacobson. I am indebted to Dr. Rountree, of the Presbyterian Hospital, for prints and copies of the roentgen-ray pictures.





FIG. 4.—Case IV. L. B. Broad penetrating ulcer, lesser curvature. Before medical treatment.

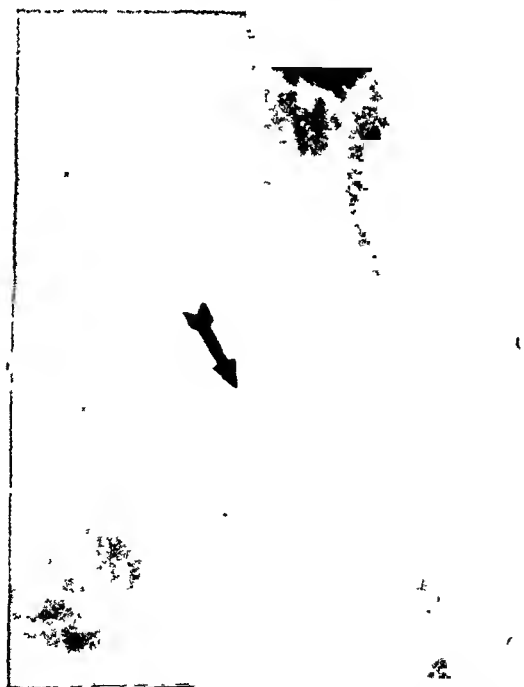


FIG. 5.—Case IV. L. B. Lesser curvature ulcer after two weeks' medical treatment. Compare with Figs. 3, 5 and 6. Note increase in depth and width of "niche."

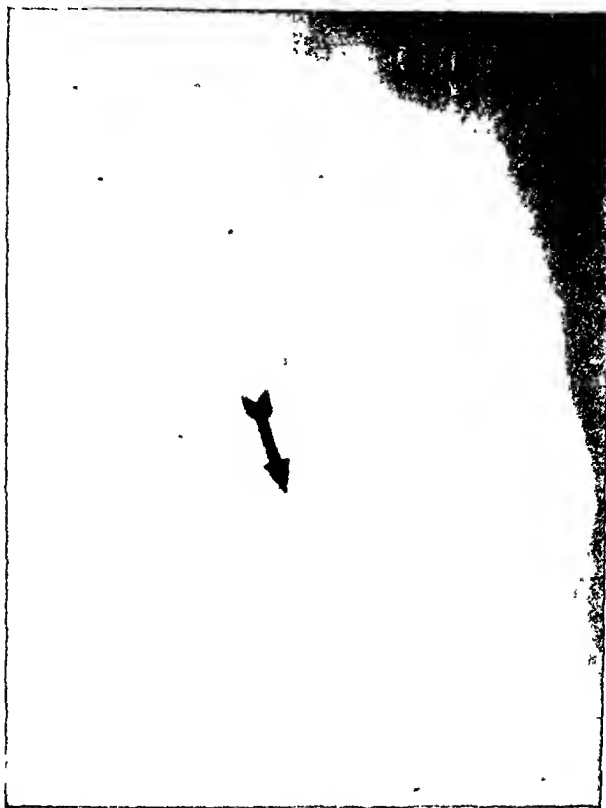


FIG. 6.—Case IV. L. B. After four weeks' medical treatment. Compare with Figs. 4, 5 and 6.



FIG. 7.—Case IV. L. B. After three months' treatment. Compare with Figs. 4, 5 and 6. Note complete disappearance of "niche," with resulting indurated area. Clinical improvement parallel.

Four weeks later a third roentgen ray was made, showing still more marked change in the lesser curvature (Fig. 6).

Three months after beginning of medical treatment a fourth roentgen ray was made, showing complete disappearance of the lesser curvature projection (Fig. 7).

While the niche itself has disappeared one could see, fluoroscopically, that the normal peristaltic waves along the lesser curvature ceased in the area of the ulcer similar to the observation of Cole,<sup>6</sup>



FIG. 8.—Case A. T. H. Penetrating ulcer of lesser curvature before treatment. Arrow indicates Haudok "niche" or pocket due to crater of ulcer filled with bismuth.

who calls this the "indurated area." In other words, apparently all that has happened is the filling up of the crater with organization tissue and possibly the transformation of a florid, penetrating ulcer into either an indurated callous ulcer or an indurated scar on the lesser curvature. The absence of the normal peristaltic waves is conclusive evidence that complete restitution with absorption of all connective tissue has not occurred.

<sup>6</sup> Loc. cit.

CASE V.—A. T. H.<sup>7</sup> a tea-taster by occupation.

*Complaint.* Late pains, vomiting, loss of weight, periodically, for five years.

*Test Meals.* Subacidity; hypersecretion; motility normal.

*Roentgen Ray.* Penetrating ulcer of the lesser curvature (Fig. 8).

Three months after treatment, during which time clinical progress was satisfactory, roentgen ray reveals slight convexity at site of original ulcer (Fig. 9).

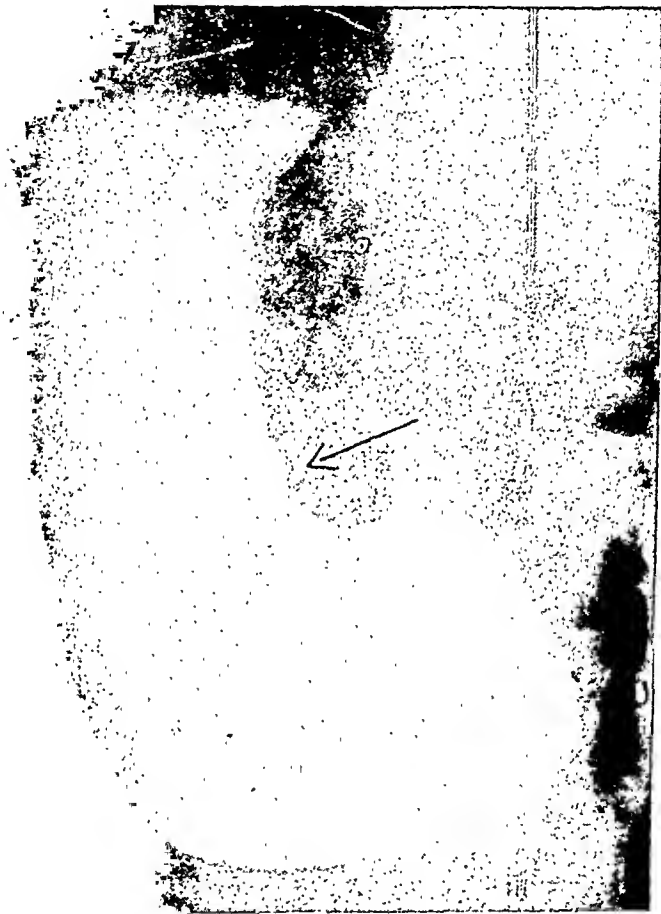


FIG. 9.—Case A. T. H. Healing of lesser curvature ulcer three months after institution of medical treatment. Arrow points to slight convexity at site of original ulcer. Compare with Figs. 8 and 10.

Four months after treatment third roentgen ray practically normal. Lesser curvature contour sharp and clean (Fig. 10).

This patient has now remained free from all gastric distress for nearly two years since treatment was begun.

CASE VI.—R. K., aged fifty-two years, a dye-worker. (Service of Dr. J. C. Friedman.)

<sup>7</sup> This case, as well as cases VI, VIII and IX, have been reported in greater detail in the Medical Clinics of Chicago, 1916, ii, 419.

*Present Complaint.* Epigastric pain for five years, vomiting, hematemesis.

*Roentgen Ray.* Penetrating ulcer of the lesser curvature (Fig. 11). Three months after treatment second roentgenological examination shows a lesser curvature defect still present, but a beginning narrowing and filling up of the ulcer crater (Fig. 12).

This patient has since disappeared from observation, but according to what scant information is at hand he is still having gastric symptoms.



FIG. 10.—Case A. T. H. Healing of ulcer after four months' treatment. Arrow points to site of original ulcer. Compare with Figs. 8 and 9.

The results of these studies bring up some rather interesting questions which may be discussed as follows:

1. It is obvious that this method is of value in studying the changes occurring in callous ulcer during the healing process.

2. The complete disappearance of the projection, *together with* parallel improvement in the patient's clinical condition, is strong presumptive evidence of healing of the ulcer.

3. The complete disappearance of the pocket cannot be interpreted as complete normal restitution of the stomach wall, but

probably is to be interpreted as simply the filling up of the ulcer crater, with probably the formation of an indurated callous ulcer or of a thickened scar. The failure of normal peristaltic waves to continue through the ulcer area is positive evidence of a remaining pathological condition.

4. The method is in no sense to be construed as an argument for or against medical treatment, but is of distinct value in the selection of cases for medical or surgical treatment; for in those cases, such



FIG. 11.—Case VI. R. K. Before treatment. Compare with Fig. 12.

as R. K. (Case VI), in which the crater could not be made to entirely disappear after prolonged medical treatment, such cases are undoubtedly worthy of surgical intervention.

5. The method does not serve to rule out carcinoma. While in my own series I have yet to experience a lesser curvature ulcer which underwent malignant degeneration (or was cancer from the start and misdiagnosed), still the possibility of overlooking an early cancer must be granted, as emphasized by Cole, Case and others.

6. Even though the ulcer crater has completely disappeared, resulting in the production of an indurated scar, permanent cure may not have been obtained. For it is possible that this scar, as in scars elsewhere in the body, remains a *locus minoris resistentiæ* may undergo secondary breaking down with the formation of a fresh active ulcer.



FIG. 12.—Case VI. R. K. After three months' medical treatment. Compare with Fig. 11. Note narrowing and filling of ulcer crater.

7. Extreme care and countless reëxaminations in all positions, including the taking, if possible, of serial plates must be insisted upon to avoid the danger of overlooking the persistence of a small crater pocket. Even with such precautions the danger of overlooking such small projections must be granted.

8. Normal peristalsis may at times be mistaken for penetrating ulcer, as was forcibly impressed upon us by the following interesting experience (Case VII).

CASE VII.<sup>8</sup>—Married woman, aged twenty-six years, symptoms for three years, consisting of late pains, hematemesis, and bloody stools.

*Roentgen Ray.* Hour-glass contraction of the stomach and indurated ulcer of the lesser curvature (Fig. 13).

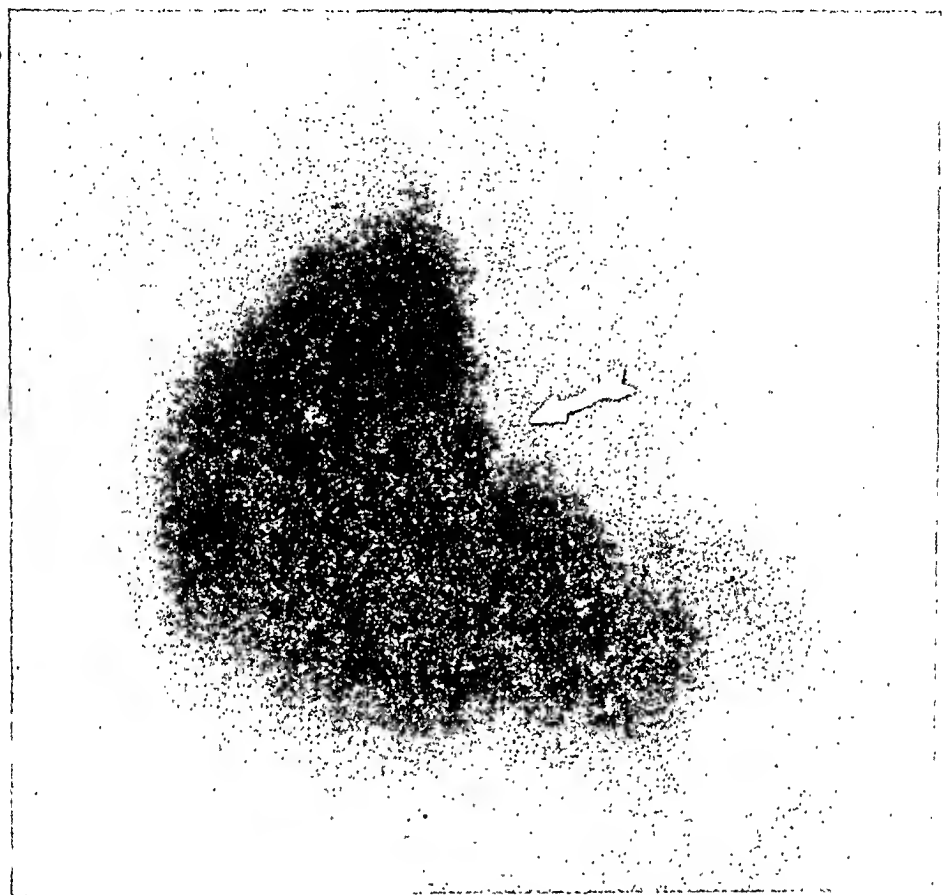


FIG. 13.—Case VII. A. S. Normal peristalsis resembling penetrating ulcer. Compare with Fig. 14.

*Operation.* (Dr. Kahlke.) “Following careful exploration of the entire stomach, anterior and posterior, cardia to pylorus, no evidence of ulcer could be found. Stomach was not opened. Appendix, gall-bladder, and ovaries, negative.”

Cole has reported a similar case (Fig. 14). However, inasmuch as exploration of the stomach was not made *from within*, it is conceivable that a small penetrating ulcer was present, but was not diagnosed. That this is not an infrequent experience can be attested to by many surgeons and roentgenologists.

<sup>8</sup> I am indebted to Dr. Kahlke for the details of this case as well as permission to report same.



II. DUODENAL ULCER.—Cole,<sup>9</sup> in 1914, described his method of serial radiography for the diagnosis of duodenal ulcers based on the recognition of a "constant deformity of the cap or sphincter caused by the induration or cicatricial contraction surrounding the crater of an ulcer or resulting therefrom."

The method described above for the control of treatment of lesser curvature ulcer has been applied to the treatment of duodenal ulcer.

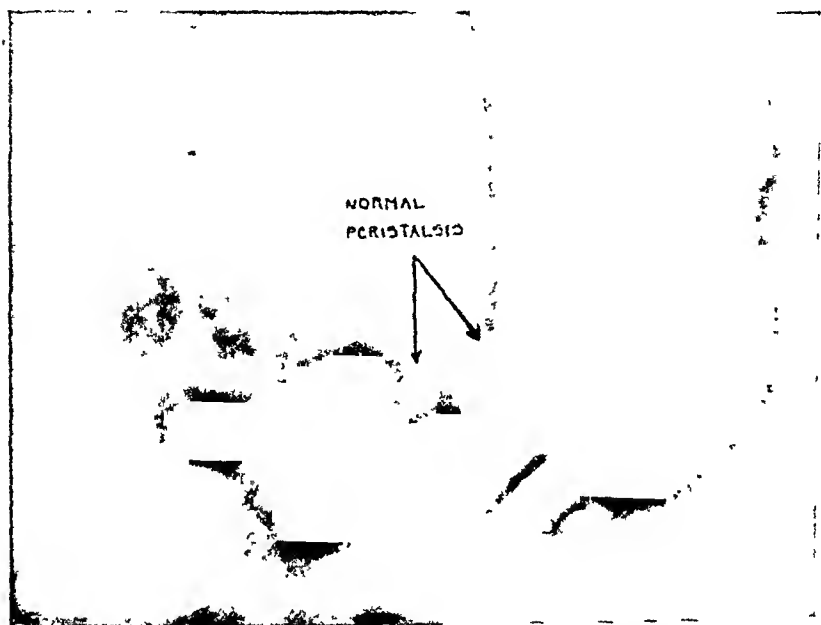


FIG. 14.—Normal peristalsis resembling ulcer. Compare with Fig. 13. (Taken from Cole.)

The following cases may be taken as representative of this type:  
CASE VIII.<sup>10</sup>—E. F. W., merchant, aged thirty-three years.

*Complaint.* Periodical for twelve years; distress after eating; black stools; vomiting of blood; loss of weight.

*Test Meals.* Hyperacidity; normal motility.

*Roentgen Ray.* Constant deformity of the duodenal bulb; motility less than six hours. Peristalsis active (Fig. 15).

Four and a half months after medical treatment with second roentgen-ray examination: The bulb was still defective, but with possible lessened degree of contraction. Peristalsis normal. No pylorospasm. Motility six hours (Fig. 16).

CASE IX.<sup>11</sup>—I. E. S., attorney, aged thirty-one years.

*Complaint.* Periodically for eighteen years, fulness late after meals, belching, gnawing sensation at night.

*Test Meals.* Hyperacidity, hypersecretion, and delayed motility.

<sup>9</sup> The Diagnosis of Post-Pyloric (Duodenal) Ulcer, *Lancet*, May 2, 1914

<sup>10</sup> Loc. cit.

<sup>11</sup> Loc. cit.



FIG. 15.—Defective duodenal cap due to chronic duodenal ulcer of twelve years' standing (case E. F. W.) Before medical treatment.

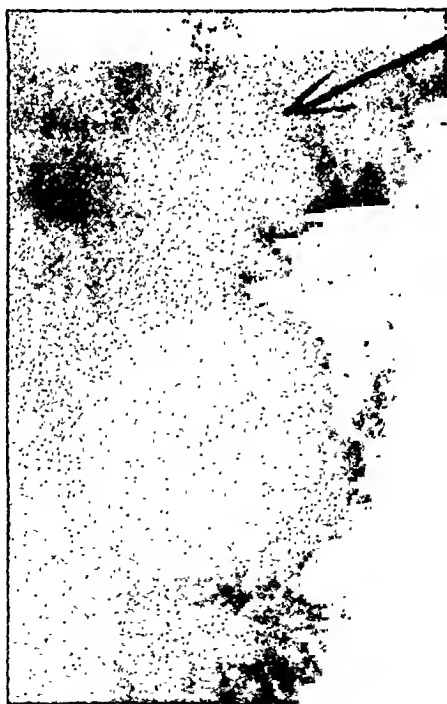


FIG. 16.—Case E. F. W. Four and a half months after medical treatment. Bulbus still defective but not quite so contracted. Compare with Fig. 15.

*Röntgen Ray.* Peristalsis slow; considerable retention in six hours. Bulbus defective (Fig. 17).

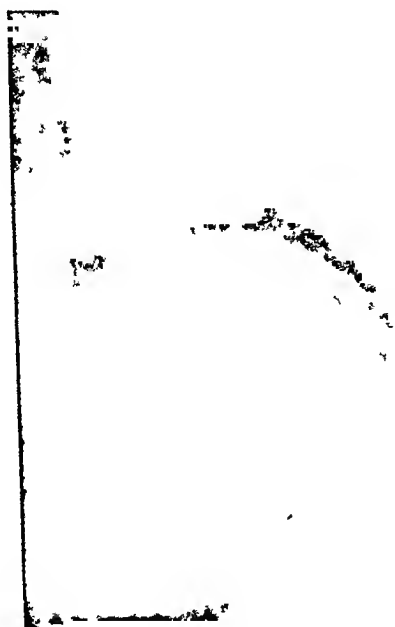
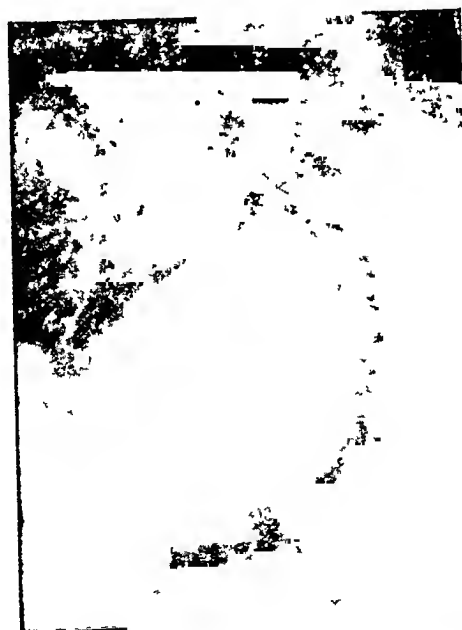


FIG. 17.—Case I. E. S. Before medical treatment. Duodenal ulcer of eighteen years' standing.



[FIG. 18. Case I. E. S. One month after medical treatment.

One month after medical treatment: Normal peristalsis, motility four hours, bulbus still defective (Fig. 18).

This method applied to cases of duodenal ulcer has not, up to the present, been productive of as many positive findings as in the case of lesser curvature ulcer. Notwithstanding it would appear that such repeated roentgenological examinations are of value and should be instituted as a routine in the medical treatment of all ulcers.

CONCLUSIONS. 1. A method of roentgenological study of the healing of gastric and duodenal ulcer is described. This method consists of repeated roentgenological studies of ulcer patients before, during, and at varying intervals after the institution of medical treatment.

2. This method is of value in the diagnosis, prognosis, control of medical treatment, and selection for surgical treatment of gastric and duodenal ulcer.

3. The method is of value in studying the pathology of the healing process in both clinical and experimental ulcer. Thus far it is not of positive value in the differential diagnosis between ulcer and cancer, although in the future it may shed some light on the much-discussed problem—the frequency of malignant degeneration of callous ulcer.

4. In the use of the method the danger of mistaking normal peristalsis for penetrating ulcer and of the overlooking of the presence of small ulcer because of incomplete or insufficient examination must be borne in mind.

5. These results are presented only as a preliminary report for the purpose of stimulating work by other men along similar lines. It is in no sense to be construed as the final word on the subject, for each new case, as it is studied, brings its own message and suggests new view-points and problems to be interpreted, thus amplifying and possibly negating the conclusions reached in the preceding cases.<sup>16</sup>

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## CHEMICAL ANALYSES OF THE STOMACH CONTENTS FROM 100 PELLAGRINS.

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INTRODUCTION. In a recent communication by Hunter, Givens and Lewis<sup>1</sup> from the laboratory of the United States Pellagra Hospital at Spartanburg, S. C., the results of gastric analyses of 29

<sup>16</sup> Most of the roentgenological examinations were made for me by Mr. Arendt, in charge of the roentgen-ray department of the Michael Reese Hospital, to whom I herewith express sincere appreciation for his assistance.

<sup>1</sup> Bull. No. 102, Hyg. Lab., Washington, 1916, pp. 42-46.

cases of pellagra in various stages of the disease were reported and discussed. The present paper covers the outcome of work along the same line, presenting data from 100 more cases. For the first time observations on a few cases at short intervals over a long period of time are reported. The investigation is also of interest in that it includes the examination of gastric contents from 24 pellagrous children.

Concerning the gastric disturbance in pellagra there is a general opinion, based on the conclusions reached by numerous students of the disease, that the absence of free hydrochloric acid is to be expected. Marie<sup>2</sup> says: "The gastric juice is often less acid in pellagrins. The hydrochloric acid is diminished." Myers and Fine<sup>3</sup> state, "Anacidity is a condition common in pellagra found in 8 of our 14 cases." Though not evident from their statements, nevertheless the opinion is generally held that free hydrochloric acid is absent, as a rule, in pellagra. Such a condition may be expected, but it is not necessarily found.

The above expectation had its foundation on the statements contained in the report of Lombroso, Filippi and Roncoroni,<sup>4</sup> on the examination of 2 cases for acidity; 10 cases (incorrectly quoted by some as 12 cases) by Cecconi<sup>5</sup> for acidity; 10 cases by Nesbit<sup>6</sup> for acidity and rennin; 20 cases by Johnson<sup>7</sup> for acidity and rennin; 14 cases by Myers and Fine<sup>3</sup> for acidity and pepsin, and the statement of Niles<sup>8</sup> concerning "analyses of 64 cases of undoubted pellagra" for acidity. These reports are of great value, but, with the exception of that of Myers and Fine, none of them throw any light upon the secretion of pepsin in the pellagrin.

Unfortunately, Myers and Fine used Rose's<sup>10</sup> method for the determination of pepsin. We believe this method to be faulty in that it demands neutralization of the gastric juice before determining the pepsin. Using Rose's original method one might find a decreased amount or entire absence of pepsin, depending upon the amount of free acid present. On this account too much reliance must not be placed upon their peptic values.

**METHODS.** During the year 1915 at the Pellagra Hospital of the U. S. P. H. S. at Spartanburg, S. C., I have examined the gastric contents of 76 cases of pellagra, and in connection with the work of the U. S. P. H. S. at a certain orphanage (E. C.) the gastric contents of 24 pellagrous children. The acidity has been determined by Töpfer's (see Hawk,<sup>11</sup>) method and the pepsin by my

<sup>2</sup> Pellagra, translated by Lavinder and Babcock, Columbia, S. C., State Company, 1910, p. 163.

<sup>3</sup> AM. JOUR. MED. SC., 1913, cxlv, 705.

<sup>4</sup> Marie, Pellagra, 1910, p. 201.

<sup>5</sup> Gazzetta degli Ospedali e delle Cliniche, 1911, xxxii, 643.

<sup>6</sup> Tr. Nat. Conf. on Pellagra, Columbia, S. C., State Company, 1909, p. 222.

<sup>7</sup> South. Med. Jour., 1911-1912, iv, 478.

<sup>8</sup> Loc. cit.

<sup>9</sup> Pellagra: An American Problem, Philadelphia, 1912, p. 77.

<sup>10</sup> Arch. Int. Med., 1910, v, 459.

<sup>11</sup> Practical Physiological Chemistry, Philadelphia, 1914, p. 440.

modification<sup>12</sup> of Rose's method. The contents of the stomach have been removed in sixty minutes and in some instances, forty-five minutes after the usual Ewald-Boas (see Sahli-Potter<sup>13</sup>) test meal. In the latter cases the gastric contents have been examined on one day after an Ewald meal and on the following day after a water meal. For the water meal the technic of Rehfuß, Bergeim and Hawk<sup>14</sup> has been used. The Rehfuß tube is given the patient, then 200 c.c. of distilled water introduced, in some cases 150 c.c., and samples for analysis removed after fifteen, thirty, forty-five, and sixty minutes.

Sufficient evidence has been obtained to show that in pellagra the water meal is just as efficient a stimulant for gastric secretion as bread and water. The conclusion is not reached from these few typical examples but from the examination of 30 cases. Table I shows the results of an Ewald meal one day and a water meal the following day.

TABLE I.—COMPARISON OF EWALD WITH WATER MEAL IN PELLAGRA.

Case No.	Date.	Total acidity.	Free hydrochloric acid.	Pepsin.	Vol., c.c.	Sample withdrawn after mins.	Meal.
52	May 29, 1915	105	86	25	72	60	Ewald.
	June 1, 1915	27	19	13	17	15	
		36	26	13	19	30	
		48	35	20	19	45	
126	Aug. 13, 1915 14, 1915	71	55	33	17	60	Water.
		85	56	31	29	60	Ewald.
		40	29	20	15	15	Water.
		56	41	25	14	30	
1	June 2, 1915 3, 1915	76	59	33	17	45	Ewald.
		87	66	33	22	60	
		84	62	25	62	60	
		33	23	13	14	15	
9	June 1, 1915 2, 1915	41	27	17	17	30	Water.
		72	51	20	19	45	Ewald.
		94	76	25	18	60	
		60	34	20	..	60	
129	Aug. 19, 1915 20, 1915	26	13	13	..	15	Water.
		37	24	20	..	30	
		60	35	33	..	45	
		42	23	33	..	60	
105	Aug. 12, 1915	19	0	0	43	60	Ewald.
		16	0	0	21	15	Water.
		17	0	0	17	30	
		20	0	0	10	45	
105	Aug. 12, 1915	21	0	0	42	60	Ewald.
		17	0	Trace	36	60	
		7	0	"	15	15	
		9	0	"	16	30	
105	Aug. 12, 1915	9	0	"	16	45	Water.
		11	0	"	24	60	

<sup>12</sup> Givens, Maurice H.: Bull. No. 101, Hyg. Lab., Washington, 1915, p. 71.

<sup>13</sup> Diagnostic Methods, Philadelphia, 1914, p. 448.

<sup>14</sup> Jour. Am. Med. Assn., 1914, lxiii, 909.

Besides the fact shown that water has produced a secretion of acid and pepsin, when it is capable of being produced in pellagra, we believe there is an explanation for it, based upon Carlson's work.<sup>15</sup> Carlson has shown that there is a continuous secretion poured out by the gastric glands in normal persons varying from 2 to 50 c.c. per hour. He states that "the autodigestion of the gastric juice itself is a probable factor in this continuous secretion." We know that when water is introduced into the stomach there is very little absorption, but that it soon passes into the intestines. Is it not then very probable that the products of autodigestion of the gastric juice are absorbed from the intestines and produce the flow of gastric juice in the case of the water meal?

Shortly after admission each patient was given either the Ewald or water meal and the stomach contents removed for examination. In some cases examinations were made at intervals of a week or longer, and this procedure continued for several months.

The results of analyses performed at the Pellagra Hospital are included in Table II, in which the cases are arranged on a basis of decreasing free hydrochloric acid; those at the orphanage, in Table III, are arranged according to duration of disease.

It would be superfluous to give in detail the clinical histories of the cases at either institution. Suffice it to say that there is as great a range and diversity of symptoms as those given in our first paper dealing with this subject. Some were severe, acute cases; some mild, acute cases; some mild, chronic and some moderately mild, chronic. Notwithstanding the large number of cases examined, and the fact that examinations were made before, during, after, and between acute attacks a careful study of the clinical conditions does not seem to permit us to correlate the absence or reduction of free hydrochloric acid and pepsin with any clinical phase of the disease. The absence of acid and pepsin does not seem to be dependent upon the number of attacks or recurrences or the duration of pellagra. This is brought out in Tables II and III, in which the number of years the patient has been subject to the disease is recorded. In Table II the word of the patient, as recorded in the case histories, is accepted. Fortunately in Table III we have the result of an examination by the same competent physician covering the periods noted.

The Ewald meal given consisted of 30 grams bread and 200 c.c. water. Of the 106 times this meal was given there were 19 instances in which more than 70 c.c. were recovered and 28 in which less than 20 c.c. were received. The remainder were within the limit of 20 to 70.

<sup>15</sup> Am. Jour. Physiol., 1915, xxxviii, 248.

TABLE II.—ANALYSES OF GASTRIC CONTENTS FROM ADULT PELLAGRINS.

Case No.	Sex.	Age, yrs.	Date.	Vol., c.c.	Total acidity.	Free hydrochloric acid.	Pepsin.	Meal.	Time, mins.	Duration of pellagra.
66	M.	30	Mar. 26, 1915	22	120	92	31	Ewald	60	1911-1915.
			April 6, 1915	17	79	61	26	Ewald	60	
			20, 1915	22	116	88	41	Ewald	60	
52	M.	34	Mar. 3, 1915	65	101	84	42	Ewald	60	1912-1915.
			9, 1915	100	84	64	31	Ewald	60	
			24, 1915	74	90	65	25	Ewald	60	
			April 6, 1915	40	89	60	21	Ewald	60	
			20, 1915	49	90	59	25	Ewald	60	
			May 29, 1915	72	105	86	25	Ewald	60	
			June 1, 1915	17	71	55	33	Water	60	
			Nov. 11, 1915	33	54	37	33	Water	60	
										Out, attack, returned.
126	M.	38	Feb. 15, 1916	9	67	46	33	Water	60	1915.
			Aug. 13, 1915	29	85	56	33	Ewald	60	
			14, 1915	22	87	66	33	Water	60	
116	M.	22	16, 1915	4	74	79	20	Ewald	60	1915.
			17, 1915	16	93	69	33	Water	60	
171	F.	22	Feb. 25, 1916	163	74	52	25	Water	60	1915-1916. 1914.
1	F.	36	Sept. 3, 1914	123	74	52	31	Ewald	45	
			Dec. 15, 1914	65	76	50	31	Ewald	45	
			Dec. 15, 1915	60	69	53	33	Ewald	45	
			Feb. 13, 1915	80	78	64	33	Ewald	45	
			15, 1915	112	76	57	41	Ewald	60	
			Mar. 24, 1915	98	73	49	31	Ewald	60	
			26, 1915	44	95	70	31	Ewald	60	
			April 7, 1915	46	80	52	21	Ewald	60	
			20, 1915	22	74	49	25	Ewald	60	
			June 2, 1915	62	84	62	25	Ewald	60	
			3, 1915	18	94	76	25	Water	60	
103	M.	29	Aug. 12, 1915	137	91	60	25	Ewald	60	
9	F.	24	13, 1915	12	80	52	25	Water	60	
			Sept. 3, 1914	32	72	47	31	Ewald	45	
			14, 1914	7	54	35	31	Ewald	45	
			Jan. 15, 1915	34	51	32	33	Ewald	45	
			Feb. 10, 1915	40	62	39	33	Ewald	45	
			26, 1915	25	57	38	40	Ewald	60	
			June 1, 1915	41	60	34	20	Ewald	60	
			2, 1915	13	42	23	33	Water	60	
			Aug. 9, 1915	38	62	37	33	Ewald	60	
			21, 1915	14	27	14	31	Water	30	
85	F.	22	May 17, 1915	19	66	49	41	Water	60	1914-1915. 1915.
70	M.	49	April 7, 1915	23	60	40	8	Ewald	60	
			21, 1915	26	71	50	16	Water	60	
			May 13, 1915	52	64	46	25	Water	60	
			Aug. 20, 1915	114	78	51	16	Ewald	60	
			21, 1915	32	61	42	25	Water	60	1914-15.
88	M.	39	May 27, 1915	58	62	36	25	Ewald	60	
			Aug. 17, 1915	32	65	32	25	Ewald	60	
95	M.	44	June 12, 1915	14	52	31	33	Water	60	1915.
150	F.	24	Nov. 8, 1915	122	47	31	21	Water	60	1914-1915.
167	F.	46	Feb. 16, 1916	40	52	34	33	Water	60	1913-1915.
160	M.	15	21, 1916	12	65	40	25	Water	60	1912-1915.
77	M.	51	April 21, 1915	15	91	68	21	Ewald	60	Do not know.
			23, 1915	10	96	74	16	Ewald	60	1914.
			May 27, 1915	4	59	28	13	Water	15	
			28, 1915	2	53	31	13	Water	15	
51	F.	30	Feb. 12, 1915	27	62	52	20	Ewald	45	
			Mar. 9, 1915	17	62	41	10	Ewald	60	
			24, 1915	12	37	12	10	Ewald	60	
			April 6, 1915	17	40	18	8	Ewald	60	
			21, 1915	8	46	25	10	Ewald	60	
			June 1, 1915	6	10	0	0	Ewald	60	1914.
59	F.	27	Mar. 3, 1915	47	52	35	25	Ewald	60	
			9, 1915	40	45	25	25	Ewald	60	
			26, 1915	9	27	7	20	Ewald	60	
			April 8, 1915	29	18	0	Tr.	Ewald	60	
			22, 1915	15	14	0	4	Ewald	60	
			June 2, 1915	49	23	2	Tr.	Ewald	60	
			3, 1915	11	6	0	0	Water	60	
154	M.	44	Nov. 8, 1915	28	68	50	13	Water	60	1915.
60	F.	22	Mar. 6, 1915	43	48	23	16	Ewald	60	1915.
			11, 1915	47	56	31	21	Ewald	60	1915.
			24, 1915	39	61	34	21	Ewald	60	
			April 7, 1915	15	62	40	16	Ewald	60	



TABLE II—continued.

Case No.	Sex.	Age, yrs.	Date.	Vol., c c.	Total acidity.	Free hydrochloric acid.	Pepsin.	Meal.	Time, mins.	Duration of pellagra.
89	F.	57	May 28, 1915	29	60	32	13	Ewald	69	1915
83	M.	68	28, 1915	4	30	9	11	Ewald	69	1911-1915
			June 1, 1915	2	58	35	11	Water	60	
			11, 1915	3 5	66	69	20	Water	39	
109	M.	7	Aug. 23, 1915	21	57	39	19	Water	45	1911-1915.
115	M.	28	10, 1915	100	56	32	10	Ewald	69	1915
115	F.	23	Oct. 6, 1915	81	51	37	17	Water	60	1913-1915.
179	F.	30	Feb. 21, 1916	5	47	30	20	Water	45	1911-1915.
151	F.	28	Nov. 4, 1915	26	46	19	25	Water	69	1915
112	M.	40	9, 1915	122	41	16	25	Water	60	1915
86	F.	26	May 21, 1915	11	15	7	17	Water	45	1915.
			June 3, 1915	124	41	18	13	Ewald	60	
117	M.	12	Nov. 9, 1915	10	41	16	19	Ewald	50	1915-1916.
113	F.	36	Oct. 6, 1915	25	40	22	20	Water	69	1911-1915
128	F.	21	Nov. 4, 1915	47	31	19	13	Water	60	1915
137	F.	33	Oct. 0, 1915	23	35	9	10	Water	45	1915.
118	F.	41	Aug. 14, 1915	103	31	19	17	Water	60	1912-1915.
61	F.	20	April 6, 1915	29	30	6	19	Ewald	60	1915
99	M.	5	Aug 23, 1915	137	30	29	10	Water	60	1914-1915
80	F.	26	May 20, 1915	173	26	18	17	Water	60	5 or 6 years.
118	F.	38	Nov. 6, 1915	3	25	8	19	Water	39	1915
63	M.	21	Mar. 23, 1915	61	21	5	16	Ewald	60	1913-1915.
161	M.	13	Feb. 15, 1916	10	32	7	10	Water	45	1915.
87	F.	28	Aug. 16, 1915	22	11	0	0	Water	69	
			17, 1915	3	40	Tr.	17	Ewald	60	1912-1915.
122	F.	46	11, 1915	25	37	0	Tr.	Ewald	69	
			12, 1915	5	20	0	Tr.	Water	69	
121	F.	21	11, 1915	89	26	0	Tr.	Ewald	60	1915.
			12, 1915	84	27	0	Tr.	Water	69	
112	F.	19	11, 1915	14	35	0	16	Ewald	60	1911-1915
			12, 1915	82	19	0	Tr.	Water	60	
133	F.	36	Oct. 7, 1915	27	21	0	10	Water	60	1911-1915
135	M.	17	2, 1915	150	21	0	10	Water	60	1915
152	F.	32	Nov. 6, 1915	21	15	0	Tr.	Water	45	1915
48	F.	33	Mar. 11, 1915	22	11	0	Tr.	Ewald	60	1912-1915
			April 8, 1915	5	39	0	Tr.	Ewald	60	
			21, 1915	3	23	0	8	Ewald	60	
			June 2, 1915	5	13	0	0	Water	45	
93	F.	33	12, 1915	35	15	0	19	Water	60	1915.
195	F.	23	Feb. 12, 1915	36	17	0	Tr.	Ewald	60	1913-1915.
			13, 1915	21	11	0	Tr.	Water	60	
11	M.	55	Sept. 3, 1914	65	11	0	0	Ewald	45	1914-1915
			8, 1911	77	12	0	0	Ewald	45	
			Oct. 17, 1914	110	9	0	Tr.	Ewald	45	
			Nov. 24, 1914	50	14	0	Tr.	Ewald	45	
			Dec. 30, 1914	112	18	0	0	Ewald	45	
			Feb. 11, 1915	70	13	0	0	Ewald	45	
			Mar. 11, 1915	56	35	7	13	Ewald	60	
			15, 1915	33	34	4	Tr.	Ewald	60	
			April 8, 1915	32	40	7	8	Ewald	60	
			May 25, 1915	14	20	0	0	Water	45	
			26, 1915	27	32	7	10	Ewald	60	
2	M.	22	Sept. 2, 1911	86	21	0	Tr.	Ewald	45	1913-1915.
			8, 1914	131	21	0	10	Ewald	45	
			Oct. 17, 1914	144	24	0	Tr.	Ewald	45	
			Nov. 21, 1914	153	14	0	Tr.	Ewald	45	
			Dec. 22, 1914	53	17	0	Tr.	Ewald	45	
			Feb. 30, 1914	100	18	0	Tr.	Ewald	45	
			Feb. 12, 1915	52	25	12	25	Ewald	45	
			Mar. 6, 1915	60	20	0	Tr.	Ewald	60	
			11, 1915	36	21	0	Tr.	Ewald	60	
			25, 1915	6	24	0	10	Ewald	60	
36	M.	55	Oct. 15, 1914	1	..	0	..	Ewald	45	1914.
			Feb. 11, 1915	19	7	0	0	Ewald	45	
			Mar. 25, 1915	27	32	5	Tr.	Ewald	60	
			April 8, 1915	28	50	18	8	Ewald	60	
			May 26, 1915	45	21	0	Tr.	Water	45	
			27, 1915	27	25	3	10	Ewald	60	
			Aug. 18, 1915	19	26	0	10	Ewald	60	
129	M.	36	19, 1915	43	19	0	0	Ewald	60	Past 5 or 6 yrs
			20, 1915	42	21	0	0	Water	60	
73	M.	36	April 13, 1915	53	27	0	0	Ewald	60	1915.
			June 1, 1915	28	10	0	0	Water	60	
			Aug 18, 1915	16	13	0	0	Ewald	60	
			19, 1915	3	20	0	0	Water	45	
			Nov. 11, 1915	9	15	0	0	Water	30	

TABLE II—*continued.*

Case No.	Sex.	Age, yrs.	Date.	Vol., c.c.	Total acidity.	Free hydrochloric acid.	Pepsin.	Meal.	Time, mins.	Duration of pellagra.
82	M.	50	May 28, 1915	9	14	0	0	Water	60	1914-1915.
81	M.	48	29, 1915	7	14	0	0	Water	30	
			26, 1915	5	20	0	0	Water	45	1914-1915.
			27, 1915	25	10	0	0	Ewald	60	
			Aug. 18, 1915	6	14	0	0	Ewald	60	
94	M.	16	June 11, 1915	186	21	0	0	Water	60	1914-1915.
50	M.	6	Feb. 11, 1915	38	21	0	0	Ewald	60	1915.
79	F.	19	May 19, 1915	116	18	0	0	Water	60	1915.
			June 3, 1915	58	18	0	0	Ewald	60	
100	M.	15	Aug. 16, 1915	25	18	0	0	Ewald	60	1915-1916.
			18, 1915	218	10	0	0	Water	60	
69	F.	34	April 8, 1915	19	25	0	0	Ewald	60	1914-1915.
57	M.	47	Mar. 24, 1915	2	10	0	0	Ewald	60	1914-1915.
			April 6, 1915	4	19	0	0	Ewald	60	
			May 26, 1915	15	28	0	0	Ewald	60	
			28, 1915	3	28	0	0	Water	30	
58	F.	40	Mar. 6, 1915	28	18	0	Tr.	Ewald	60	1915.
55	F.	28	3, 1915	65	20	0	0	Ewald	60	1909-1915.
84	M.	23	May 11, 1915	30	21	0	0	Ewald	60	1910-1915.
149	F.	42	Nov. 11, 1915	18	14	0	0	Water	45	1912-1915.
144	F.	27	4, 1915	21	11	0	0	Water	45	1912-1915.
155	F.	30	8, 1915	78	9	0	0	Water	60	1915.
132	M.	57	Oct. 4, 1915	14	15	0	0	Water	60	1911-1915.
140	M.	40	2, 1915	18	21	0	0	Water	60	1915.
141	M.	59	2, 1915	22	22	0	0	Water	60	1913-1915.
131	M.	52	Aug. 24, 1915	6	10	0	0	Water	45	1913-1915.
176	F.	35	Feb. 16, 1916	48	16	0	0	Water	60	1915.
164	M.	32	15, 1916	22	12	0	0	Water	45	1915.
153	F.	31	21, 1916	15	16	0	0	Water	45	1911-1915.

From the work of Boldyreff<sup>16</sup> one would expect some more or less constant relationship between the acidity and the volume of

TABLE III.—ANALYSES OF GASTRIC CONTENTS FROM PELLAGROUS CHILDREN.

Case No.	Sex.	Age, years.	Vol., c.c.	Total acid.	Free hydrochloric acid.	Pepsin.	Meal.	Sample withdrawn after mins.	Duration of pellagra.
200.	M.	12	20	93	73	25	Water	40	1 year.
205.	M.	8	29	51	34	25	Water	60	1 year.
202.	M.	13	7	44	19	10	Water	60	1 year.
207.	M.	13	8	42	21	20	Water	60	1 year.
201.	M.	10	31	40	22	10	Water	60	1 year.
204.	M.	6	5	40	20	10	Water	60	1 year.
203.	F.	6	13	35	24	10	Water	20	1 year.
206.	F.	15	17	38	20	20	Water	60	1 year.
214.	M.	12	13	50	30	33	Water	60	2 years.
216.	M.	14	5	42	29	17	Water	60	2 years.
209.	M.	8	5	34	21	10	Water	60	2 years.
211.	M.	8	10	29	11	10	Water	60	2 years.
213.	M.	6	112	26	9	10	Water	60	2 years.
215.	M.	13	63	25	12	13	Water	60	2 years.
210.	M.	10	98	20	0	Tr.	Water	60	2 years.
212.	M.	7	23	19	8	10	Water	20	2 years.
208.	M.	11	72	12	0	0	Water	60	2 years.
217.	M.	10	97	58	43	20	Water	60	3 years.
218.	F.	16	51	51	33	20	Water	60	3 years.
219.	M.	17	6	87	62	33	Water	60	4 years.
221.	M.	15	46	61	43	17	Water	60	4 years.
220.	M.	9	32	46	24	10	Water	60	4 years.
222.	M.	13	70	12	0	0	Water	60	4 years.
223.	M.	10	9	59	35	17	Water	40	5 years.

<sup>16</sup> Quart. Jour. Exper. Physiol., 1914, viii, 1.

fluid in the stomach. He has shown conclusively that gastric contents of a high degree of acidity are not permitted to enter the intestines until the acidity has been reduced to about 0.14 per cent. hydrochloric acid. He states "The more rapidly the acidity diminishes the more quickly the stomach empties itself." Accordingly one would expect in the case of a high acidity to find a rather large volume of fluid in the stomach and the reverse with a low acidity. No doubt a good part of the water was in the stomach, because of the high acidity due to the secretion of hydrochloric acid. In the case of no secretion of hydrochloric acid, from our ideas concerning the stay of water in the stomach, we would expect the stomach shortly to empty itself. In the cases here reported there is no constant or definite relationship between volume and acidity; that is to say, with a high acidity there are many instances at the end of an hour with a small volume in the stomach, some with a large volume; cases with low acidity of large and small volume; cases with no acidity of large and small volume.

ACIDITY. Before making the divisions later referred to it will be necessary to set some limits. The following table shows the normal standard after the Ewald meal as accepted by the authors whose names are opposite:

	Vol., c.c.	Total acidity.	Free acidity.
Butler <sup>17</sup> . . . . .	20 to 50	40 to 60	27 to 55
Sahli-Potter <sup>18</sup> . . . . .	30 to 70	..	40 to 55
Emerson <sup>19</sup> . . . . .	30 to 70	40 to 60	20 to 60
Farr and Goodman <sup>20</sup> . . . . .	..	40 to 60	
Goodman <sup>21</sup> . . . . .	..	40 to 60	

We concur in the opinion expressed by Bergeim, Rehfuß and Hawk<sup>22</sup> that these values are too low. They do not offer another standard, but state that their total acidity values ranged from 50 to 120, with an average of 77 after their water meal. They have found higher values than the clinicians quoted above in perfectly normal individuals after an Ewald meal. Reviewing their work, and taking it in conjunction with some of our own,<sup>23</sup> it is here proposed to offer as limits of the standard for a normal total acidity 50 to 80. We mean to consider the acidity as subnormal if below the figure 50 and the free hydrochloric acid deficient if below 18. When above 80 we prefer to consider the acidity as of their "hypersecretory type," since no other findings or the clinical

<sup>17</sup> *Diagnostics of Internal Medicine*, New York, 1913, p. 670.

<sup>18</sup> *Loc. cit.*

<sup>19</sup> *Clinical Diagnosis*, Philadelphia, 1913, p. 353.

<sup>20</sup> *Arch. Int. Med.*, 1908, i, 648.

<sup>21</sup> *AM. JOUR MED. SC.*, 1908, cxxxvi, 734.

<sup>22</sup> *Jour. Biol. Chem.*, 1915, xix, 345.

<sup>23</sup> Givens, M. H.: *Bull. No. 101, Hyg. Lab., Washington*, 1915, p. 71.

evidence warrant calling these cases of hypersecretion. A review of Tables II and III gives:

10 cases of the hypersecretory type or . . . . .	10 per cent.
22 cases of the normal type or . . . . .	22 "
29 cases of the subnormal type or . . . . .	29 "
39 cases with absence of HCl . . . . .	39 "

Pellagra favors neither age nor sex in bringing about the condition found in the stomach; that is to say, free acid and pepsin may be absent in the young or old, male or female. If one desired to make a more discriminating separation a survey of Tables II and III would permit of the selection of the following types of gastric secretion as found in the pellagrin:

High free acidity with normal pepsin.  
 Normal free acidity with normal pepsin.  
 Disappearing free acidity with disappearing pepsin.  
 Normal free acidity with low pepsin.  
 Low free acidity with normal pepsin.  
 Low free acidity with low pepsin.  
 No free acidity with trace of pepsin.  
 No free acidity with no pepsin.

Previous to the present investigation enough cases have not been studied by any one person to allow such a grouping. This shows the great number of possible conditions one would be liable to find in a given case.

As will be seen from the number of types of secretion the free hydrochloric acid and pepsin did not run hand in hand. In the majority of cases in which free acid was absent pepsin also was absent. Accepting 25 to be the low limit for pepsin, we find it normal in 20 cases, subnormal in 32, deficient (10— to trace) in 21, and absent in 23.

A record of the presence of bile in the contents has been kept, but it is not considered worth adding, and thereby further complicating the two tables for two reasons: In the first place it is practically impossible to introduce the tube without causing the patient to gag more or less. In order to overcome this tendency as much as possible, coöperation (on the part of the patient) was sought, but, owing to the class here treated, little was rendered. On this account it is very likely that the strong contraction of the abdominal muscles has forced duodenal contents into the stomach. As a matter of fact the records will bear out this statement. In the second place, as Carlson<sup>24</sup> and Boldyreff<sup>25</sup> show, when there is free normal acidity in the stomach for a few minutes the pyloric sphincter dilates and the duodenal contents enter to neutralize the increasing acidity.

As to how long an attack of pellagra lasts, or whether one attack overlaps onto the next attack or recurrence, it does not seem

<sup>24</sup> Loc. cit.

<sup>25</sup> Loc. cit.

possible to say. On this account it was not considered justifiable to attempt to correlate the number of attacks or recurrences with the presence or absence of acid and pepsin. On the other hand, the number of years the patient has shown lesions of pellagra is recorded, but this does not throw any light on the subject. For example, Cases 66 and 132 have had pellagra five years. In the former there is a "hypersecretory type" of acidity with normal pepsin, whereas in the latter there is no free acid or pepsin. The same thing is shown in the case of the two children, Cases 219 and 222. Nesbit<sup>22</sup> says, "The indications are that in pellagra, as in all adynamic and asthenic diseases, the hydrochloric acid and ferments of gastric juice progressively diminish." Three cases have been found which will confirm his finding and show the disappearance of free hydrochloric acid more gradually, and in less time than he reports, with the added disappearance of pepsin.

Nesbit's cases.			Writer's cases.				
Case No.	Date.	Free hydrochloric acid.	Case No.	Date	Total acidity.	Free hydrochloric acid.	Pepsin.
III.	Aug., 1908	35	51	Feb. 12, 1915			
	April, 1909	10		Mar. 9, 1915	62	52	20
	Aug., 1909	4		24, 1915	62	41	10
IV.	Aug., 1908	8	59	April 0, 1915	37	12	10 -
	May, 1909	0		21, 1915	40	18	8
				June 2, 1915	46	25	10
VI.	Jan., 1908	24	77	Aug. 8, 1915	18	0	0
	June, 1909	0		Mar. 3, 1915	16	0	0
				9, 1915	52	35	25
VII.	Sept., 1907	39	77	26, 1915	45	25	25
	April, 1908	20		April 8, 1915	27	7	25
	Oct., 1908	8		22, 1915	18	0	20
				April 21, 1915	14	0	Tr.
				23, 1915	91	0	Tr.
				May 27, 1915	96	68	21
				28, 1915	59	74	16
				29, 1915	53	28	13
					37	31	13
						17	

Conversely, attention is called to Cases 52, 1 and 9, who were watched over eleven and a half, nine and eighteen months respectively, and practically no change was seen. Case 52 is particularly interesting in that he left the hospital, had a severe attack, and returned between the examinations of June 1, 1915, and November 11, 1915, and is still within limits as to acid and pepsin. Cases 14, 2 and 36 were watched over nine, seven and eleven months respectively, and there was nothing to indicate a return to a normal secretion of the stomach, notwithstanding that from a clinical point of view these patients did not show any obvious symptoms

<sup>22</sup> Loc. cit.

of pellagra at the time of the last gastric examination. This is the only record of which we know concerning such a condition in pellagra.

It is not necessary to consider the dietary of these cases, since no difference was noticed in any of the cases under diets of various sorts.

Johnson,<sup>27</sup> in an examination of 20 cases, found that in 14 lacking hydrochloric acid there was a diarrhea, while in no one case with hydrochloric acid was there diarrhea except in one due to a transient cause. He also seemed to think the diarrhea was lessened if rennin were present. A careful review of our cases does not yield such a consistent relation. We have found diarrhea present both in the presence and absence of free acidity.

The following table gives a *résumé* of the conditions found by the various investigators referred to in this paper:

Authority.	Number of cases.	Free hydrochloric acid.							
		Excessive and normal.		Subnormal.		Deficient.		Absent.	
		No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.
Nesbit . . . . .	10	..	..	2	20	4	40	4	40
Cecconi . . . . .	10	..	..	..	..	..	..	10	100
Johnson . . . . .	20	2	10	4	20	1	..	14	70
Myers and Fine . . . .	14	2	14	3	21	1	7	8	57
Niles . . . . .	68	15	23	..	..	31	48	18	28
Hunter, Givens and Lewis	24	8	33	2	8	2	8	12	50
Givens . . . . .	100	32	32	21	21	8	8	39	39

Although reported previously, Cases 1, 2, 9, 14 and 36 are included in Table II on account of many subsequent observations. Accordingly the number of cases of Hunter, Givens and Lewis<sup>23</sup> has been changed to 24. With the exception of Niles,<sup>29</sup> who does not give the analyses but makes only a summary statement, all of the other cases have been made to conform to the standard set in this paper for normal, subnormal, and deficient acidities. Reviewing the above available data one sees that the variations in a small number of cases are such as would lead often to erroneous opinions, especially in regard to the absence of free hydrochloric acid.

SUMMARY. A careful review of the 100 cases examined, covering over 300 analyses for acidity and pepsin, permits of the following summary:

1. No definite relation can be found between the absence of pepsin and free hydrochloric acid, and sex, age, duration of pellagra, and clinical symptoms.

2. The gastric secretion of children is disturbed along the same general line as that of adults.

<sup>27</sup> Loc. cit.

<sup>23</sup> Loc. cit.

<sup>29</sup> Loc. cit.

3. Free hydrochloric acid and pepsin do not seem to be absent as often in children as in adults.

4. Although the tendency is for acid and pepsin to disappear hand in hand, such is not always the case.

5. It is believed that pepsin and free acid are present more often than has been expected.

## THE INCIDENCE OF CHRONIC FOCAL INFECTION IN CHRONIC DISEASES.

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ALTHOUGH there has been a large amount of literature on the subject of focal infection, the medical profession has been, on the whole, slow to adopt the principles laid down by Rosenow and Billings. On this account I have reviewed briefly what has been done in the medical clinic of the University of California Hospital, hoping to emphasize the importance of this work.

According to this principle many acute and chronic diseases of heretofore unknown origin are believed to be and have in many cases been actually demonstrated to be of bacterial origin. This has been proved by the introduction of new bacterial methods, tissue cultures, and new media which more nearly approach the human tissues from which the bacteria are grown. Tissues which in former years under older methods were found sterile, on culture now yield bacteria in large numbers. The streptococcus in one or the other of its forms has been the most frequently isolated organism. Introduction of these freshly grown cultures of streptococci into animals has shown that the particular organism in question has acquired, to a certain extent, a selective affinity for certain tissues. That is to say, a culture of streptococci from a human stomach ulcer when injected into large numbers of animals will cause a relatively large percentage of stomach ulcers in the animals injected, though many other lesions may also be caused. This strain of streptococcus has acquired an affinity for stomach tissue. The same may be said for streptococci isolated from appendicitis, arthritis, endocarditis, and other lesions. These same organisms isolated from the stomach ulcer may in many cases be found in some chronic focus in the same patient, usually a lesion which does not drain properly. These tooth abscesses, chronic tonsils, sinus and prostatic infections harbor bacteria which must get into the blood stream at such times when the resistance is low and gradually acquire an affinity for some particular tissue which is in time attacked either violently, as is the case in an acute purulent chole-

cystitis, or at recurring intervals, as in the case of the joints. In the case of the more chronic diseases concerned these fresh attacks by bacteria from the focus of infection are synchronous with exacerbations of the disease; in the more distant tissues for which the bacteria have acquired an affinity, and these exacerbations are accompanied by such general symptoms as fever, malaise, sweating, weakness, general aching, and anorexia. Such invasions may probably occur without the medium of a particular focus when the general symptoms are the same, but the bacteria do not, as a rule, localize in any particular tissue. As will be shown later we are unable in many cases to locate a diseased focus in many chronic diseases where, according to the principle, one should exist. Then we must either suppose that it has escaped us, that it has already been eliminated, or that some deeper inaccessible structure is serving in its place.

Endocarditis, myocarditis, nephritis, arthritis, myositis, ovaritis, several nervous diseases of hitherto unknown origin, bronchial asthma, ulcer of the stomach and duodenum, cholecystitis, appendicitis, iritis, and erythema nodosum have all been caused in animals by the injection of bacteria grown from chronic foci found on the patients suffering from these diseases.

In the medical clinic of the University of California Hospital we have been especially interested in the subject of focal infection, not only because of its explanation of the cause of diseases whose etiology was hitherto unexplained, but also because of the hopeful field that it opened up as regards therapeutics. There are many limits to the successful and thorough study of such a problem in dispensary work. We must see the large percentage of the patients as ambulatory cases and so lack the advantages of placing them in the hospital for study. We are hampered by the ignorance and poverty of the patients, and especially is the work difficult because of our inability to follow the patients for the considerable length of time which is necessary in order properly to observe results. Our results in a majority of the cases, then, show the coincidence of focal infection with the different diseases studied rather than the clinical cure or amelioration of the disease. In a number of cases, however, the therapeutic results have been very good; in a few cases they have been brilliant. The foci which lend themselves most readily to our work are the teeth and the prostate. We have found that the outward appearance of the teeth is frequently no indication of root abscess, which is almost always surely shown by roentgen plates. Many of the necrotic stumps have tooth abscesses but not all of them do. Crowned teeth may be infected at the roots, but one is sometimes surprised to find a mouth full of crowned teeth that from the roentgen ray all have healthy roots. On two occasions we have insisted on the removal of teeth because the plate showed a distinct area of rarefaction at the root apex, and pus has not been



found. These are accidents which are bound to occur, but we have found that even with a positive report from the roentgen-ray department one should rely on the judgment of a competent dental surgeon when he declares the tooth to be, nevertheless, sound. On one occasion a dentist refused to pull a tooth which had very evidently a root abscess, because the patient had no pain and tenderness about the tooth. Fortunately the dental clinic concurred in our diagnosis and the tooth was removed there. The prostate, of course, lends itself very readily to examination and the presence of pus in the secretion is determined in a moment under the microscope. We have decided the question of infection of the accessory nasal sinuses with the aid of the roentgen ray and the clinical examination in the nose and throat department, though it must be acknowledged that it is difficult at times to say whether or not there is a slight infection here. Tonsils are many times evidently infected. At other times it is impossible to say whether they are healthy or not. Unless they were obviously the site of an infection we have tended to leave these until the other foci were eliminated, generally because of the reluctance of the patients to part with them. We believe them to be a much less frequent focus of infection in adults than in children.

I have gone over the histories of the patients seen in the last two and a half years with the diagnosis of ulcer of the stomach or duodenum. There were 30 of these cases. In 3 the records made no mention of teeth or tonsils; 12, or 40 per cent., had definite alveolar abscesses; 11, or 40 per cent., had carious teeth or enlarged and infected tonsils; 1 had chronic prostatitis, and 4, or 14 per cent., had no demonstrable focus. Thus a chronic focal infection was demonstrated in 13 cases or nearly 50 per cent., and very probable in an additional 40 per cent. In the 4 remaining cases the tonsils were small and smooth; but in view of the known difficulty of determining whether or not a tonsil is infected until its removal it is impossible to say there was no focus. Ulcer patients are almost invariably much benefited by dietary measures, are usually able to go about their work, and soon disappear from view. We have been able in most cases to have the infected teeth removed, but in the short period of observation have found it impossible to say whether the removal of the focus has prevented recurrence of the ulcer. So far no tonsils have been enucleated for ulcer cases, though this should be urged when other foci have been removed and recurrences still occur. It is hoped that in a few years' time many of these patients will return and that more definite data will be obtained as to the effect of the clearing up of these tooth abscesses.

There have been 12 cases of acute or subacute arthritis, and in these are included those patients who complained of aching joints whether there was demonstrable swelling or not. In 8, or 66 per cent., a chronic focus was demonstrated. One of these cases, a subacute, multiple arthritis, cleared up immediately following tonsillectomy,

another cleared up after drainage of an accessory nasal sinus. One of the cases in this group was a girl, aged seventeen years, with a subacute arthritis of the right foot of several months' duration. The joint improved the day after drainage of the alveolar abscess by extraction, and in ten days the patient wore a shoe for the first time in three months. The remaining cases in this group failed to return after diagnosis. In 3, or 25 per cent., there were probable foci in the shape of carious teeth or infected and enlarged tonsils, but the patient failed to return for roentgen-ray examination and was lost track of. Only 1 case failed to show a focus. This was a woman, aged fifty-four years, with syphilis, some pyorrhoea, but no definite alveolar abscesses, and small smooth tonsils.

In 40 cases there was a diagnosis of chronic arthritis, and in this group are included all those showing any considerable change in the spine or other joints. These cases form a respectable percentage of the out-patient work, and it seems certain that for some reason in many of them there has been no record of the diagnosis, perhaps because it was a secondary one. Fourteen of these records are incomplete as regards specific statements about teeth, tonsils, prostates, etc., and are therefore omitted from the group, though a good many were described as having all teeth missing, and the fact that the tonsils escaped mention probably means that they were negative. Some of these therefore should be classed in the group in which no focus was found. Twenty-six cases are then left in which the investigation was complete. In nineteen of these, or 73 per cent., a chronic focus was demonstrated, and in this group it was always an alveolar abscess or chronic prostatitis. In an additional 4, or 15 per cent., a chronic focus was probable, that is, the tonsils were infected and enlarged, the teeth in bad condition, but with no record of roentgen-ray examination. In 3 cases, or 11 per cent., there was no demonstrable focus. It is not maintained that in every case of chronic arthritis a focus will be found or that the focus in each case is the actual cause of the lesion in the joints. Many of these patients were sixty or over and are described in the records as having lost all their teeth. From what we see of these people we are almost justified in assuming that they have had one carious tooth after another, one alveolar abscess after another, until finally the last teeth are extracted. The joint changes are undoubtedly initiated many years before the patient is seen at the clinic and have progressed by that time to actual bony change. The most we can hope for at that time is to prevent any further progress by removing what foci are found. The frequently repeated phrase "*small atrophied tonsils*" found in the records of the physical examinations makes it seem probable that the tonsils are very, very rarely at fault in a patient over sixty, and that in the chronic hypertrophic or atrophic type of arthritis little is to be expected by their removal. Many of the cases of chronic arthritis of the spine are characterized

by recurring attacks of stillness and pain on movement, sometimes by slight constitutional symptoms which are spoken of by the patient as lumbago. In these a focus will almost surely be found, and most often located in the prostate. These cases do very well indeed after appropriate treatment for the local infection, but this must be persisted in sometimes for months. By eradicating the prostatitis we can prevent the attacks which mark the progress of the disease in the spine, leaving the patient to get along fairly comfortably with what permanent changes he has already acquired. In this connection it is interesting to remember that the spine changes are often overlooked until the sacro-iliac joint becomes abnormally loose, perhaps in an attempt to compensate for the rigidity of the lumbar spine in forward flexion. Abnormal motion or strain in the sacro-iliac joint may cause pain over the joint or down the back of the leg, and this may be what brings the patient to the clinic. Nathan has described, in a recent article, neurological changes found in cases of chronic polyarthritis and spondylitis. These are explained by the epidural exudate which he found on the anterior surfaces of the bodies of the vertebræ and in the intervertebral notches and the resulting nerve pressure. In at least 2 cases of chronic lower spinal and sacro-iliac disease there have been associated neurological changes, in 1 case a loss of the patellar reflex on the side involved, and in another a complaint of spasticity on the side of the sacro-iliac lesion. In another case, that of a young man, there was bilateral loss of patellar and Achilles jerks associated with very marked angulation in the lumbar spine and an absolutely negative spinal fluid examination, although the patient had a perforation of the septum and probable syphilis.

There have been 4 cases of chronic gall-bladder disease, 2 associated with alveolar abscesses, 1 with infected tonsils, and 1 with a chronic prostatitis. Most of these cases probably have gall-stones, but the complicating attacks of cholecystitis originate in the chronic focus of infection found so often in the teeth.

A number of other conditions, such as loss of weight, myocardial insufficiency, herpes, headaches, and neuritis, have been found associated with chronic focal infection, but the number in each group is too small to be of any value and the connection perhaps too uncertain.

The figures given above do not, of course, prove any causal relation between chronic focal infection and the various chronic diseases mentioned, but they do show the occurrence together of the two in a large percentage of the cases. As seen in out-patient work the diseases associated with these focal infections are usually well advanced and beyond hope of a cure. The most for which we can hope is to ameliorate symptoms. It is notably in the acute and sub-acute cases that the good results have been obtained, and it is appreciation of this fact that makes this principle a far-reaching one.

Patients who complain of backache, aching joints, indefinite heart symptoms, or who occasionally show albumin, casts, or red blood cells in the urine, should be carefully examined, and foci when found should be cleared up. Such treatment may prevent the final development of chronic polyarthritis and spondylitis, myocardial insufficiency, or nephritis.

In conclusion, 84 per cent. of ulcer patients, 66 per cent. of acute or subacute cases of arthritis, 73 per cent. of the chronic cases of arthritis, and 100 per cent. of the gall-bladder cases have been associated with chronic focal infections. The acute and subacute cases have responded well after removal of the foci, even to the point of absolute cure. The chronic cases, when we have been able to follow them, have in many cases had less pain and no further progression of the disease. A thorough understanding of the principles involved makes clear the nature and cause of diseases hitherto only poorly understood and opens up a more hopeful therapeutic prospect where before we have had to treat symptomatically.

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## A REPORT ON THE ELECTROCARDIOGRAPHIC STUDY OF TWO CASES OF NODAL RHYTHM EXHIBITING R-P INTERVALS.

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THE rarity of clinical cases of nodal rhythm showing an *R-P* interval seems to us to be sufficient reason for this communication.

The term nodal rhythm is applied to a mechanism in which the seat of impulse formation lies in the *A-V* node or conduction tissues. Although in all hearts the node of Tawara has the inherent power of rhythmic stimulus production, this power is usually kept in abeyance because of the greater rhythmicity of the sino-aortic node, the heart responding to that pacemaker which exhibits the highest rate of impulse formation.

Wilson<sup>1</sup> describes two clinical types of nodal rhythm which, in the sense of Lewis, he calls heterogenetic and homogenetic. The former partakes of the character of a paroxysm of tachycardia with sudden onset and abrupt offset, the heart not under the control of the extrinsic cardiac nerves; the homogenetic type is characterized by a comparatively slow rate, gradual onset and offset, with the heart subject to nerve control.

Our first case belonged to type 1, of which type we find but 6 cases in the literature. These are recorded by Lewis,<sup>2</sup> Rihl,<sup>3</sup>

<sup>1</sup> The Production of *A-V* Rhythm in Man after Administration of Atropin, Arch. Int. Med., 1915, xvi, No. 6, 989-1006.

<sup>2</sup> Auricular Fibrillation and its Relationship to Clinical Irregularity of the Heart, Heart, 1910, i, 306-372.

<sup>3</sup> Paroxysmal Tachycardia Accompanied by the Ventricular Form of Venous Pulse, Heart, 1910, ii, No. 2, 127-147.

<sup>4</sup> Ueber atrioventriculäre Tachycardia beim Menschen, Deutsch. med. Wchnschr., 1907, xxxiv, 632-634.

Cohn,<sup>5</sup> Hume,<sup>6</sup> and Falconer and Dean.<sup>7</sup> The patient was referred to us by Dr. De Witt B. Nettleton, to whom we are indebted for the privilege of publishing the following case history:

CASE I.—W. L. C., male, white, aged fifty-seven years, widower, retired manufacturer.

*Chief Complaint.* Attacks of palpitation with rapid heart action.

*Present Illness.* For twenty years patient had had attacks of acceleration and palpitation, lately increasing in frequency. The attacks might come at intervals of every few days, or as often as fifty times in one day. For several months during the past summer the patient had had no attacks, but two weeks ago they had returned. Until recently the attacks seemed to bear no relation to exercise or emotion, but of late they occurred more frequently during fatigue. Although the patient usually walked three or four miles a day, if he walked during an attack extreme fatigue resulted. With the onset of acceleration, there developed an extreme degree of palpitation, and, in the more recent attacks, also a sense of precordial oppression not before present. There was no cyanosis nor dyspnea; no noticeable cough nor edema. Attacks might last a few seconds or for hours, the longest was between three and four hours' duration. Rate during the attack was about 120; the rhythm was regular. If he were standing during an attack, occasionally the patient felt faint. Flatus followed the attacks.

The onset was usually spontaneous, but might be brought on by such change in posture as stooping or by a distended stomach. The palpitation began with a sudden acceleration of heart rate—before this moment the heart beat had been slow, below the threshold of consciousness—the acceleration continued for a variable period, then ceased just as suddenly, was followed by a pause, then a heart thump or two, and finally a resumption of the normal rate without palpitation. The patient can frequently check an attack by holding the breath, by continued deep breathing, or by lying down; these measures, however, are not always efficacious. The effect of vagus pressure was never tried. On the morning of the last examination, lying down caused a short paroxysm, and later a short walk of 300 feet brought on another attack. The patient stated that very rarely was the heart rate accelerated without symptoms.

*Past History.* Patient had had malaria in early manhood and typhoid at thirty; frequent sore throats but no definite tonsillitis. There had been no scarlet fever nor diphtheria. Renal calculus passed at fifty-two; infection of right kidney followed. He had an

<sup>5</sup> A Case of Paroxysmal Tachycardia, *Heart*, 1910, ii, No. 2, 170-176.

<sup>6</sup> A Polygraphic Study of Four Cases of Diphtheria with a Pathological Examination of Three Cases, *Heart*, 1913, v, No. 1, 25-44.

<sup>7</sup> Observations on a Case Presenting a long A-C Interval, Associated with Short Paroxysms of Tachycardia arising in the Junctional Tissues, *Heart*, 1912, iv, No. 2, 137-144.

attack of acute appendicitis, with operation at fifty-three. No cardiorespiratory symptoms between attacks of tachycardia. Troublesome tinnitus was frequent.

*Habits.* Good.

*Family History.* Negative.

*Physical Examination.* Well-developed and well-nourished middle-aged man. Except for the cardiorespiratory-vascular system the examination was practically negative. The heart was not enlarged to percussion. Apex was felt in V interspace about 0.5 cm. to the left of the midclavicular line. Heart sounds were very faint; no murmurs audible;  $A_2 > P_2$ , but not accentuated. There was slight sclerosis of right temporal and radial arteries, not excessive considering the age of the patient. In general the heart sounds were of regular rhythm, although occasionally at the apex a pause approximately equal to the period of two beats was noted. No heart sounds were audible during this pause, which the patient recognized as an irregularity, because of the heart throb which followed. On the first examination of the patient in June, 1916, the pulse rate was 68; the blood-pressure: systolic 118, diastolic 68. On August 1, during the period of acceleration without palpitation or other symptoms, the rate varied between 105 and 120; blood-pressure: systolic 96, diastolic 65. November 22 the pulse rate averaged 95 between attacks, while in two different paroxysmal attacks it was 136 and 122 respectively. The lungs showed a few scattered medium moist rales. There was present moderate stethoscopic edema.

Urine. Acid: 1.015 to 1.020; albumin, 0 to very slight trace; sugar, 0; occasional hyaline cast; slight trace of pus. Phenolsulphonephthalein test 78 per cent. excreted in two hours.

The first electrocardiogram on this case was taken June 20, 1916, at which time the patient had no acceleration of rate (Fig. 1). It showed a normal origin and conduction of impulses with an average rate of 76 beats per minute. The  $P$ - $R$  interval was 0.16 second; the  $P$  waves were upright in leads I and II, diphasic in lead III. There was a slight left ventricular preponderance.

August 1 several electrocardiograms were obtained. During the taking of one of these the patient was having an acceleration of rate without any symptoms, such as he said "occurs about once in a thousand times." This electrocardiogram (Fig. 2) showed a simple acceleration with a rate of 107 to the minute. The  $P$  waves were upright, as before, in leads I and II (the only leads taken), while the  $P$ - $R$  interval was unchanged, 0.14 to 0.16 second, indicating a normal origin and conduction of impulses. Another plate, taken the same day, showed a rate of 76 with a  $P$ - $R$  interval of 0.16 second and upright  $P$  waves.

November 22 the patient was again electrocardiographed during normal periods and during two typical attacks of acceleration, such

as have been described in the case history. During the normal periods the rate varied from 73 to 100, averaging about 95; the *P* waves were upright in all leads and preceded the ventricular deflection by 0.16 second.

During the attacks the rates were 136 and 122 respectively, the *P* wave was invert and following the *R* wave, with an *R-P* interval of 0.1 second. There was no change in the ventricular complex during the paroxysms, the onset and offset of which were abrupt.



FIG. 1.—(No. 210-1, lead II.) Electrocardiogram of Case I taken during a period of normal mechanism. The rate was 76. *P-R* interval = 0.16 second. The ordinates of all electrocardiograms shown represent  $10^{-4}$  volt, the heavy and fine abscissæ represent time intervals of 0.2 and 0.04 second respectively.

With the return to normal in the last paroxysm the rate dropped suddenly from 122 to 73, the *P* wave became upright, at first low then gradually increasing in height, and there was an immediate return to a *P-R* interval of 0.16 second (Fig. 3). Between the paroxysmal attacks of tachycardia the regular rhythm was occasionally interrupted by a premature beat of junctional origin which showed the normal form of ventricular complex, except that it was

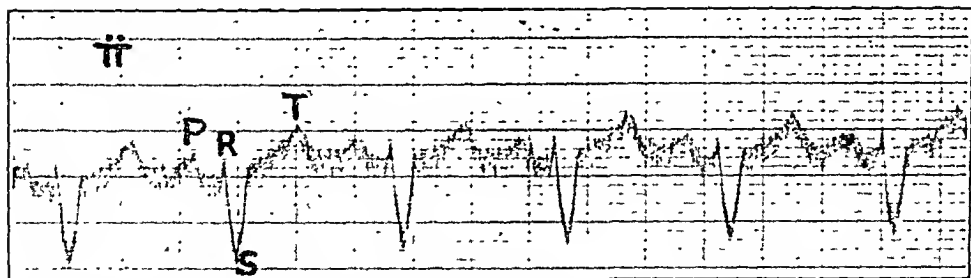


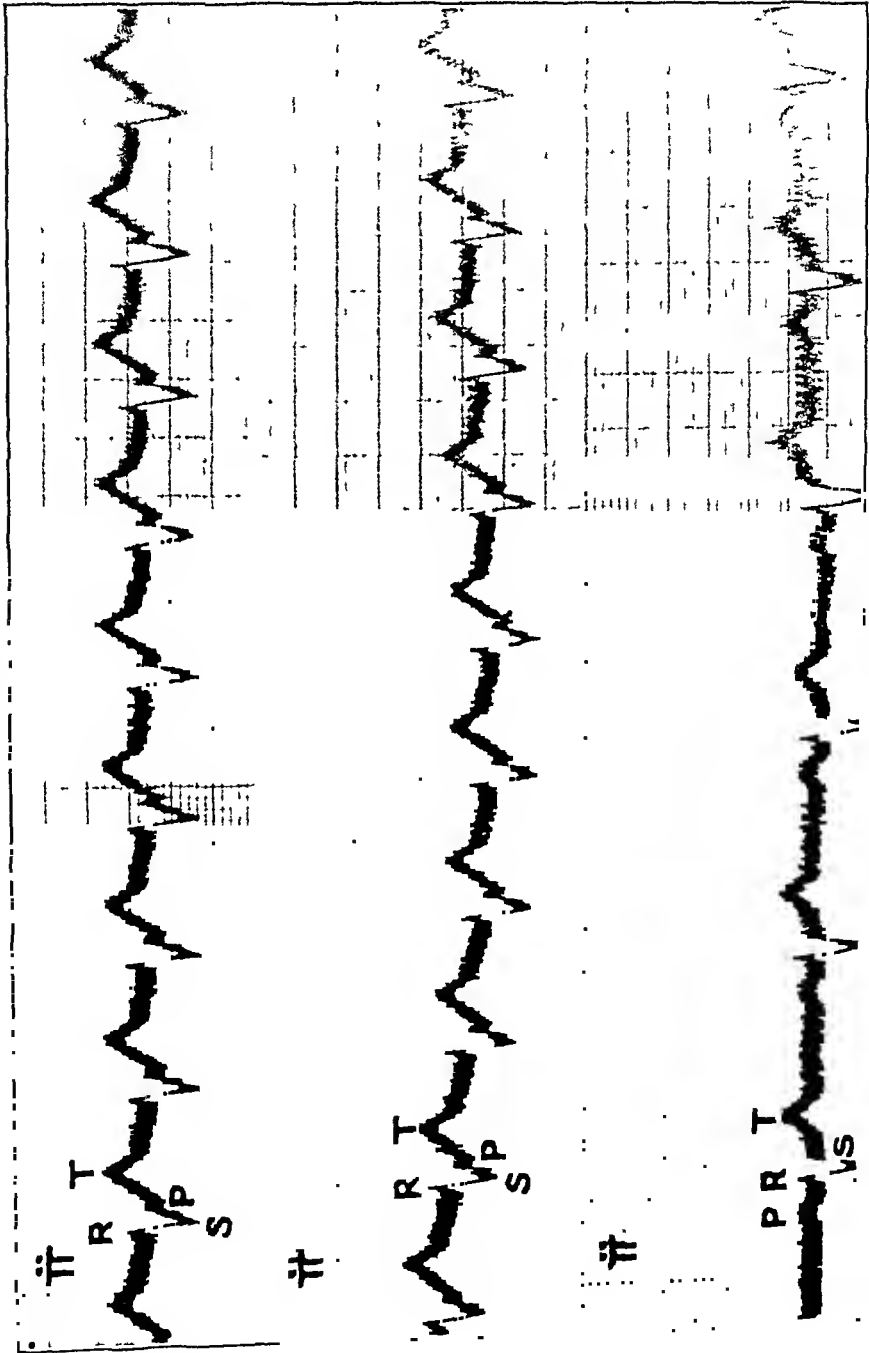
FIG. 2.—(No. 210-5, lead II.) Electrocardiogram of Case I taken during a period of normal mechanism with acceleration. No subjective symptoms. The rate was 107. *P-R* interval = 0.14 to 0.16 second.

of diminished size (Fig. 4). The *P* wave was invert and followed the *R* wave by 0.1 second. The pause following the premature beat was almost compensatory. During these premature beats no sounds were heard over the precordium and no pulse could be felt at the wrist.

The second case described cannot be definitely classified. There



are several points in favor of the impulse formation being of hetero-  
genetic type, others in favor of a homogenetic origin. The nodal  
rhythm developed while the patient was under ether anesthesia,



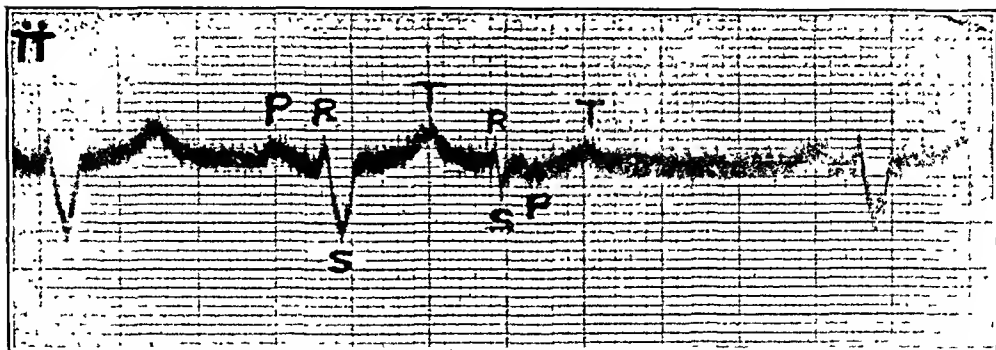


FIG 4.—(No. 210-10a, lead II, film.) Electrocardiogram taken a few minutes after Fig. 3. A junctional premature beat is shown in which the ventricular complex is smaller than but of the same general conformation as that of the normal cycles, the *P* wave being invert and following the *R*.

and neither the onset nor offset of the abnormal mechanism was observed. The clinical history of this case follows:

CASE II.—Mrs. M. W., aged thirty-six years, white; married; housewife. Admitted to St. Francis Hospital, service of Dr. H., January 2, discharged January 30, 1917.

*Chief Complaint.* About fourteen months before admission patient had noticed gradually increasing general weakness, which became so marked that any effort caused extreme fatigue; she had been confined to her home during that period, spending most of the time in a chair or in bed. The weakness had steadily increased despite rest in bed and medical treatment. For two and one half years preceding she had noticed occasional weakness, but it had not been so severe. About eight months before coming to the hospital the patient tried to increase effort and took two walks of about 300 yards each; both were followed by a "fainting attack" similar to others she had had for the past sixteen years. These attacks always began with a feeling of thoracic oppression, as though there was a weight on the chest; patient's lips and fingertips became very cyanotic; a cyanotic lacework appeared over the skin; the hands grew cold; and patient became very dyspneic and weak. Because of weakness she had accustomed herself to lying down; she had lost consciousness only two or three times, and that many years before. She never had had convulsions, but attacks

#### EXPLANATION OF FIG. 3

(No. 210-10, lead II.) Electrocardiogram of Case I taken during a typical attack of paroxysmal tachycardia. The entire figure is of lead II, the three parts being taken in immediate succession. The end of the paroxysm occurred while the camera plate was being raised for the taking of the third portion of the figure. The postparoxysmal pause was observed but not recorded. A period of about five seconds elapsed between the end of each third of the figure and the beginning of the succeeding third. The heart rate during the paroxysm was 122 with an *R-P* interval of 0.1 second. The rate after the paroxysm was 73 with a *P-R* interval of 0.16 second. Note the similarity of the ventricular complex during and after the attack, except as it is modified by the superimposition of the invert *P* during the paroxysm. There is a progressive increase in the height of *P* immediately following the paroxysm.

ended with a "nervous chill." During these attacks, because of the dyspnea and weakness, patient lay in a semicomatose condition, knowing what went on about her, but unable to speak. The extreme dyspnea usually lasted from fifteen minutes to an hour, during which time there was gradual improvement. The weakness lasted two or three days. During these attacks, according to statement of husband, the pulse was usually "better" than between them; by this statement he means stronger and faster; it was never below 44 nor over 60, but usually irregular. The description of this irregularity is much like that of a premature beat, followed by compensatory pause, while the description of the irregularity of pulse noticed between attacks is more like an actual "missed beat." Pulse has been slow during the patient's entire life, usually below 60. Last year, for one month, pulse is said to have been constantly between 18 and 25, and was noted on several occasions by her attending physician at these rates. She never has had palpitation nor edema. For years she has had slight unproductive cough, not increased with dyspnea. Her nervousness had been noticed for seven years; she became easily excited and had "internal quivering," followed by increased weakness and dyspnea. Frequently she had paresthesia of arms and legs, usually bilateral, but never any local paresis nor paralysis. The paresthesia usually lasted fifteen to twenty minutes, and was often, though not always, associated with dyspnea. Recently the feeling of "pins and needles" had been noticed whenever the patient awoke at night. There was always dysmenorrhea; menses were irregular. The "cardiac attacks" noted above usually come just before or just after the menstrual period. Nycturia once; diuria 6 to 7. No dysuria nor hematuria; chronic constipation; occasional gaseous eructation. For the past six months the patient had had an eruption on the face.

*Past History.* Measles, mumps, and varicella as child. At the age of two years the left eye was injured and the sight of this eye was destroyed. Frequent attacks of tonsillitis until ten years ago, when they ceased.

At sixteen years had the first "fainting attack," similar to that described in present illness. These attacks had occurred about twice a year since that time, but more often since present illness. There had been frequent partial aphonia since girlhood.

At nineteen years, she had a severe hemorrhage, but whether gastric or pulmonary was not known, and no details were obtainable.

In 1911 she had left-sided dry pleurisy and a "nervous breakdown," because of which she was in a hospital for fifteen weeks.

For twenty years has had dyspnea on slight exertion (one flight of stairs) even between attacks.

*Occupational History.* School teacher and supervisor for sixteen years until two years ago; since then has had household duties. She always worked very hard.

*Family History.* Practically negative. Married two years. Never pregnant.

*Physical Examination.* Slightly built, poorly-nourished woman lying flat in bed in no discomfort. Skin of left half of face showed many discrete and confluent dark red papules; only one papule on right side of face.

Mucous membranes of good color; not cyanotic.

Left eye showed internal squint; patient could only distinguish light with this eye.

Oral cavity and throat negative, save for crowded teeth and dental work.

Lungs were negative.

Heart outline was small to percussion. R. B. D., 3 cm.; L. B. D., 7 cm. from midsternal line in IV interspace. Apex felt in fourth space, 7.5 cm. from midsternum. Supracardiac dulness 4.5 cm. wide. Heart sounds were of good quality, regular except for a very rare "missed beat," during which pause no sounds were audible over precordium. This pause was about twice the length of that between the regular beats. At pulmonic area a soft, blowing systolic murmur was audible; not transmitted.  $P_2 > A_2$  not accentuated. No thrills. Pulse was of fair volume and low tension; the walls of the radials were not sclerosed. Rate, 56 to 63. Blood-pressure: systolic, 100; diastolic, 60.

Abdomen: Negative. Knee-jerks: Lively. Extremities: No edema.

Pelvic examination by Dr. Huggins revealed an infantile ante-flexed uterus and undersized ovaries.

*Laboratory Findings.* Blood: Hemoglobin, 80 per cent.; red blood cells, 4,460,000; white blood cells, 7400. Morphology of reds and differential essentially normal.

Urine: Negative.

Phenolsulphonephthalein test: Sixty-seven per cent excreted in two hours.

Wassermann (blood): Positive.

Wassermann on husband's blood negative (never received anti-specific treatment).

*Course.* Temperature usually subnormal.

Pulse varied from 40 to 126, usually between 40 and 70 with a tendency to remain at about 60. During most observations the pulse was regular except for the occasional presence of a long pause, during which no heart sounds were audible. The frequency of these pauses varied from day to day, sometimes recurring every few beats, at other times unrecognizable during a prolonged period of observation. When the pauses were most frequent the pulse was slowest. The slowest rate observed by writers was 41, although the husband is said to have observed a rate of 32 shortly previous to this time.

January 20, under ether, patient had dilatation and curettage of uterus, with introduction of stem pessary by Dr. Huggins. The

pulse and blood-pressure findings at this time will be given in Table I. Pessary later came out and was reinserted January 27 without ether. During stay in hospital patient complained of general weakness like that which had preceded admission. She had several periods of paresthesia, as previously described, but objective examination at such times revealed nothing definite.

The results of electrocardiographic examinations will be discussed in the body of the paper. Patient discharged January 30, only slightly improved.

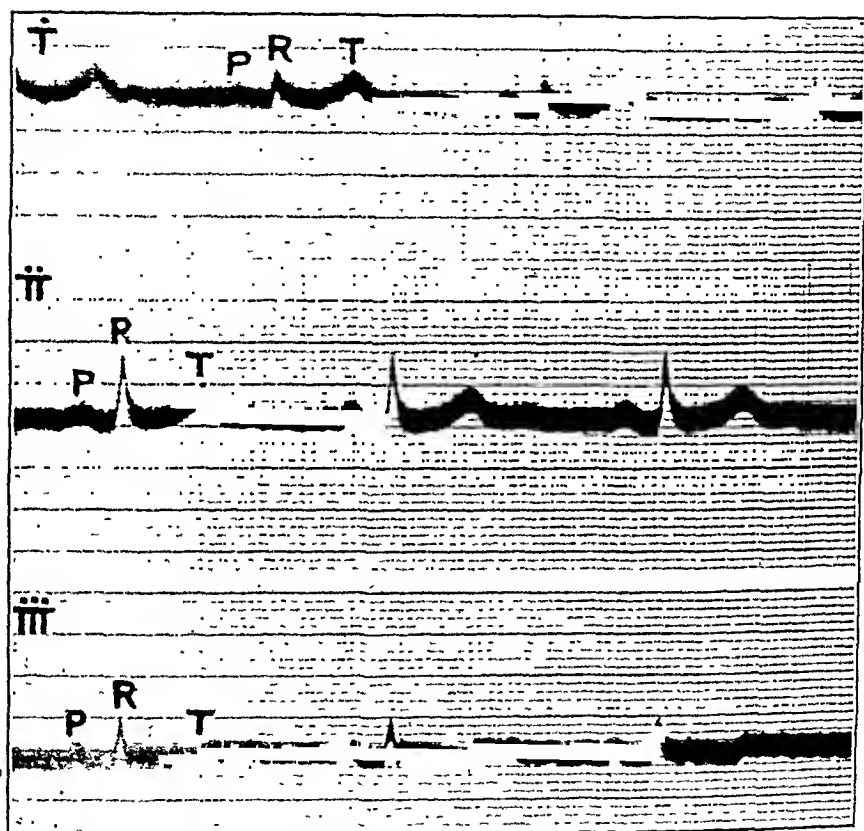


FIG. 5.—(No. 308-11, leads I, II, III.) Electrocardiogram of Case II taken during a period of regular heart action. There is a slight sinus arrhythmia. Rate = 55.  $P-R$  interval = 0.16 second.

On seven different occasions during the stay in the hospital, electrocardiographic examinations were made. On all these occasions, except while the patient was under ether, the electrocardiograms showed a marked sinus arrhythmia, frequent sinoauricular heart-block, and bradycardia (Figs. 5 and 6). The slowest rate obtained by electrocardiograph was 41, the longest  $R-R$  interval was 2.04 seconds. The  $P-R$  interval varied from 0.16 to 0.18 second during the normal rhythm. The  $P$  wave was

always upright in leads *I* and *II* and upright or diphasic in lead *III*. In the electrocardiogram taken immediately after the operation, January 20, while the patient was still under complete ether anesthesia, the mechanism was different from that at any other

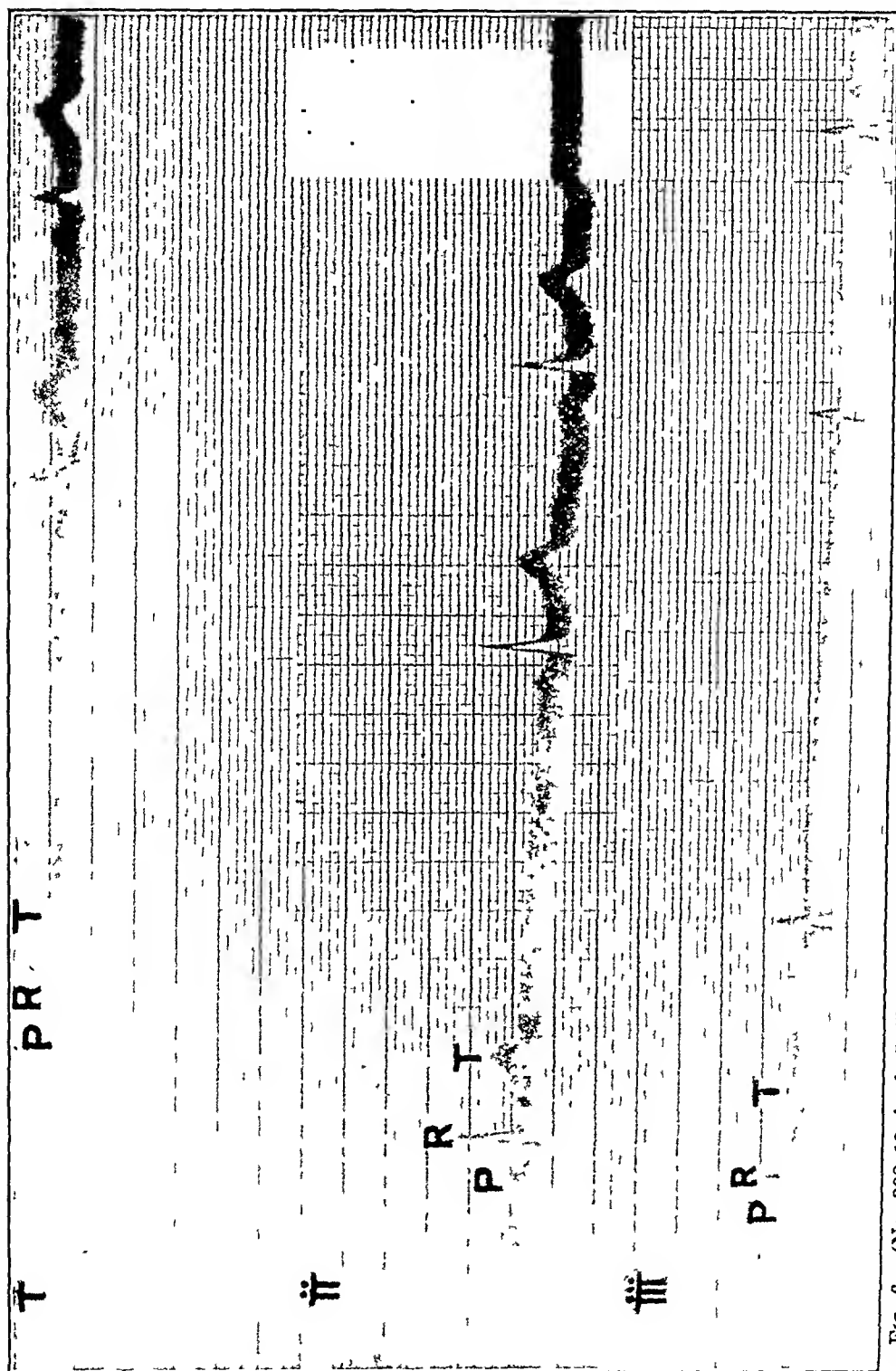


FIG. 6.—(No. 308-12, leads I, II, III.) Electrocardiogram of Case II taken during a period of slow and irregular heart action. There is evidence of frequent sino-auricular block. The average rate is 41, the longest R-R interval = 2.04 seconds. The P-R interval = 0.10 to 0.18 second.

examination (Fig. 7). There was no marked change in the ventricular complexes except that the *R* waves were slightly higher, while the *T* of lead III tended more toward inversion. The *P* wave, however, instead of preceding the *R* followed it with an *R-P* interval of 0.06 to 0.1 second. The contour of the *P* was also changed, for in this plate it was of smaller amplitude and shorter duration, while in all leads it varied from upright to diphasic. The rate of

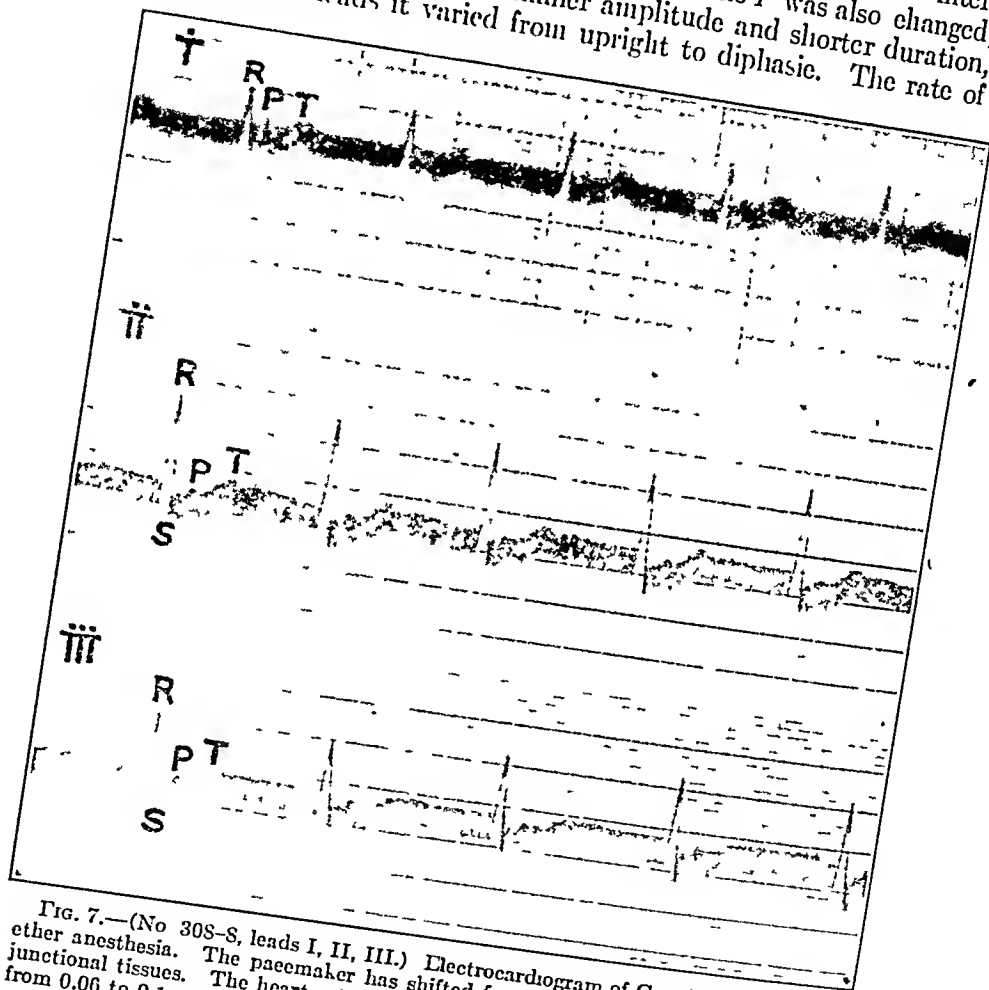


Fig. 7.—(No 308-S, leads I, II, III.) Electrocardiogram of Case II taken during ether anesthesia. The pacemaker has shifted from the sino-auricular node to the junctional tissues. The heart rate varies from 97 to 83. The *R-P* interval varies from 0.06 to 0.1 second. The ventricular complex is unchanged.

the heart in this electrocardiogram varied from 83 to 97, with an average of 92, whereas the fastest rate with the heart responding to the normal pacemaker was 63. As one might expect because of the enhanced rate the duration of ventricular systole during the nodal rhythm was shorter than that during the normal mechanism, 0.28 to 0.32 and 0.4 to 0.44 second respectively. Unfortunately the record taken during the operation was not developed until several hours later, so that the change in mechanism

was not known at once. For this reason the series is not so complete as it might be desired. As soon as it was known there had been a shifting of the pacemaker the patient was again electrocardiographed, but not until five hours after the preceding plate had been made. Meanwhile there had been complete recovery from the anesthetic. This latter group of plates showed a return to the normal mechanism, the *P* upright in all leads, *P-R* interval 0.14 to 0.16 second, the rate 63, with a slight sinus arrhythmia, but no evidence of sino-auricular block. All the deflections at this time were very small. The next electrocardiograms showed a return to the condition before the operation, a condition that persisted throughout all remaining electrocardiograms.

A table of the pulse and blood-pressure readings on the day of operation may be of interest (Table I). There was a marked variation in the intensity of the systolic sounds over the brachial artery while blood-pressures were being taken during the operation. The intensity varied with the phases of respiration, being much the louder during inspiration. This phasic variation was most marked during early anesthetization, but it persisted throughout the period of etherization and for some time thereafter.

We have already stated that the first case cited was of the heterogenetic type. The fact that the paroxysms could sometimes be stopped by the patient either by holding the breath or by rapid, deep breathing would seem to indicate that the control of the extrinsic cardiac nerves was not entirely lost. However, as these effects were inconstant, we must beware of the *post* and *ergo propter* fallacy. The other criteria for the recognition of junctional paroxysmal tachycardia, namely, rapid rate, sudden onset and offset, shortened, absent, or negative *P-R* interval, inversion of *P*, normal ventricular complex, and postparoxysmal pause were all present.

In the second case neither onset nor offset was pictured or observed. From the pulse rates as given in Table I, because of the length of the intervals between observations, we cannot be certain whether or not the change was sudden. However, inasmuch as the rate during the taking of the electrocardiogram varied from 97 to 83, while there was a general tendency toward a gradual fall both before and after the electrocardiogram was taken, the supposition is that the change was not abrupt. The rate, although much more rapid than during response to the sinus pacemaker, was not excessively rapid when the electrocardiogram was being taken. However, it may be presumed that the nodal rhythm was also present at an earlier stage of the operation when the rate was 120. From the data at hand we cannot determine whether the rhythm in this second case was of heterogenetic or homogenetic origin. However, as the latter origin is much the more common we favor the supposition that the disturbance was of the homogenetic type in spite of the fact that the comparatively rapid rate is in favor of the former.



TABLE I.

Jan. 20, 1917. Time.	Systolic.	Diastolic.	Pulse- pressure.	Pulse rate.	Character of pulse.	Notes.
9.00 A.M.	104	66	38	63	Regular	Before operation.
9.30	..	..	..	..	..	Morph. sulph. gr. $\frac{1}{4}$ ; atrop. sulph. gr. $\frac{1}{32}$ .
10.30	..	..	..	80	Regular	Ether begun.
10.50	112	95	17	120	"	Partial anesthesia.
10.53	140	110	30	110	"	Partial anesthesia.
10.55	125	110	15	114	"	Complete anesthe- sia
11.00	132	70	62	126	"	Dilatation of cer- vix begun.
11.05	130	65	65	123	"	Curettage.
11.08	..	..	..	95	"	Operation finished.
11.10	..	..	..	..	..	Electrocardiogram taken; complete anesthesia.
11.15	135	95	40	..	..	Patient removed from table.
11.30	..	..	..	90	"	Patient in her room.
11.40	..	..	..	80	"	
12.00	..	..	..	61	"	Patient partially recovered from ether.
12.05 P.M.	..	..	..	70	"	
12.30	..	..	..	80	"	
12.40	..	..	..	68	"	
12.50	..	..	..	70	"	
1.05	110	70	40	60	"	Still drowsy from ether.
1.15	..	..	..	68	"	
1.25	..	..	..	70	"	
1.55	..	..	..	68	"	
2.20	..	..	..	68	"	
4.15	100	65	35	68	"	Completely recov- ered from ether; electrocardio- gram taken.
6.00	..	..	..	..	..	Morph. bimecon- ate, gr. $\frac{1}{4}$ s.c.
8.00	..	..	..	60	"	Feeling comfort- able.

The question of etiology is an interesting one—several factors require consideration. Thus the patient had been given a hypodermic of morphin (gr.  $\frac{1}{6}$ ) and atropin (gr.  $\frac{1}{150}$ ) one hour before etherization was begun. We know of no observations in regard to morphin administration in connection with observed instances of shifting of the pacemaker to the conducting tissues. The case is different with regard to atropin. Thus, Wilson was able to induce nodal rhythm by vagus stimulation in normal persons who had received preliminary injections of atropin (1 mg.). This result could usually be obtained only when stimulation was applied eight to twenty minutes after the injection. In our case the electrocardiogram was taken one hour and forty minutes after the injection, and but twenty minutes after the marked rise in rate noted in Table I. This suggests that the shifting of pacemaker was not

the result of the morphin-atropin injection alone. Furthermore, the administration of the morphin-atropin mixture is a routine measure preliminary to operations in St. Francis Hospital, and no other cases of nodal rhythm have been observed by us over a series of 21 cases in which electrocardiograms have been taken during anesthesia. That asphyxia is capable of causing a shifting of pacemaker to  $A-V$  node has been shown by Lewis, White, and Meakins<sup>8</sup> who induced nodal rhythm in cats by this method. However, since our patient took the ether well and at no time showed any signs of asphyxiation we must look further for the cause of the changed mechanism. Wilson<sup>9</sup> cites 3 cases in which forced respiration caused the pacemaker to change from the  $S-A$  to the  $A-V$  node. As the respirations were increased under ether administration this forcing may have been a partial factor in the changed mechanism. However, the data is too scanty to permit of definite conclusions being drawn. The effect of the ether itself is not fully known, but our other cases show that, at least, it is not commonly a cause of  $A-V$  rhythm.

In most cases of nodal rhythm the  $P$  is invert; but its inversion is not an essential characteristic. Thus Meakins<sup>10</sup> has shown that the  $P$  wave may be polyphasic, and that in only 8 of his 9 experiments did the auricular complex begin with a downstroke. Lewis and Allen<sup>11</sup> have described a case of premature beats arising in the  $A-V$  tissues in which case the  $P$  wave was upright and of normal contour; from this fact, together with the varying  $P-R$  intervals, they conclude that the auricles were responding to the normal pacemaker while the ventricles were responding to an impulse arising low in the  $A-V$  bundle. This case, however, is not analogous to ours. In our first case the  $P$  wave was invert; it was upright or diphasic in our second. We believe that both are true cases of nodal rhythm, the auricles and ventricles both responding to the new pacemaker.

Wilson divides each of his previously mentioned types of nodal rhythm into three subtypes dependent upon the origin of the impulse: (1) those with a shortened  $P-R$  interval,  $P-R$  0.1 second or less; (2) those in which the  $P-R$  interval is absent,  $P-R$  equals 0; (3) those in which the  $P-R$  is negative, that is, changed to an  $R-P$  interval. The origin is supposed to be progressively lower in the auriculoventricular tissue in types 1 to 3; the latter is the lowest and also clinically and experimentally the least common. White<sup>12</sup> believes that an  $R-P$  interval may be due either to a low

<sup>8</sup> The Susceptible Region in  $A-V$  Conduction, *Heart*, 1914, v. No. 3, 289-298.

<sup>9</sup> Three Cases showing Changes in the Localization of the Cardiac Pacemaker Associated with Respiration, *Arch. Int. Med.*, 1915, xvi, No. 1, 86-97.

<sup>10</sup> Experimental Heart-block, with Atrioventricular Rhythm, *Heart*, 1914, v. No. 3, 281-288.

<sup>11</sup> An Instance of Premature Beats arising in the Auriculoventricular Bundle of a Young Child, *Am. Jour. Med. Sc.*, 1913, cxlv, No. 5, 667-671.

<sup>12</sup> A Study of  $A-V$  Rhythm following Auricular Flutter, *Arch. Int. Med.*, 1915, xvi, No. 4, 517-535.

position in the *A-V* tissues or to resistance in the auriculo-nodal junction or to both together. Hering,<sup>13</sup> however, has shown that the greatest delay in conduction through the junctional tissues occurs in the node of Tawara. The general belief is that with an *R-P* interval the origin of impulse is in or below the node. In both the cases we have described in this paper there was an *R-P* interval indicating a low origin in the junctional tissues; likewise, in both cases the ventricular complexes were unchanged, except for modification by the superimposition of the *P* wave, indicating that the impulses originated above the division of the main stem of the His bundle.

The slow rate of the sino-auricular rhythm in the second case is interesting in conjunction with the case of junctional paroxysmal tachycardia described by Lewis, in which the rate between attacks was usually about 50, with an occasional rate as low as 37. In regard to that case Lewis said that the slow rate occurred during a "sinus arrhythmia." Although the published curves do not show a sino-auricular block, we are led to question whether such a block were not occasionally present as in our case.

Eyster and Meek<sup>14</sup> have shown that the average rate of rhythmic discharge of the auriculoventricular tissues in dogs is about 67 per cent. of that of the sino-auricular node; in cats the relationship is closer but the rate is still below that of the *S-A* node; in man the automatic rhythmicity of the nodal tissues is likewise lower than that of the normal pacemaker. Hence, White suggests that when the rate of a nodal rhythm is rapid, that rapidity indicates more than a mere depression of the sino-auricular node; it indicates stimulation of the auriculoventricular tissue. The fact that the rates during nodal rhythm in both of our cases were high compared with the rates during the normal mechanism points therefore to some abnormal stimulation of the new pacemaker.

SUMMARY. Two cases are presented in which electrocardiographic study showed the development of transient nodal rhythm. The first case exhibited junctional premature contractions and typical attacks of paroxysmal tachycardia such as had extended over a period of twenty years; the second presented marked sino-auricular block, and under ether anesthesia there developed a paroxysm of auriculoventricular rhythm.

During the paroxysms of abnormal rhythm there was present in both cases an *R-P* interval indicating an origin of impulses low in the conduction tissues. The comparatively rapid rates during the paroxysms of auriculoventricular rhythm suggest an abnormal stimulation of the junctional tissues.

<sup>13</sup> Nachweis, dass die Vergögerung der Erregungsüberleitung zwischen Vorhof und Kammern des Säugerthierherzens im Tawaraschen Knoten erfolgt, Arch. f. d. ges. Physiol., 1910, cxxxi, 379-401.

<sup>14</sup> Experiments on the Origin and Conduction of the Cardiac Impulse. VII Sinoventricular and Sino-auricular Heart-block, Arch. Int. Med., 1917, xix, No. 1, 117-139.

**PATHOGENESIS OF INFANTILE SCURVY: AN HYPOTHESIS.\***

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I. ETIOLOGY. Originally infection and toxemia played prominent parts in the theoretical etiology of scurvy, but during the past two decades there has been practically universal agreement among individuals working on the problem of scurvy that it is not due to an infection or to a toxemia, but to the destruction of some substance in the diet whose presence is necessary to prevent the development of the characteristic scorbutic symptoms. However, during the past year Jackson and Moody<sup>30</sup> reported observations which, according to McCollum,<sup>44</sup> are suggestive of the presence of a toxic substance of bacterial origin injuring the bloodvessels. McCollum<sup>44</sup> himself very recently stated that he is convinced that guinea-pigs on a diet of oats and milk suffer from scurvy because of the constipating character of the diet. I personally doubt, however, whether McCollum's guinea-pigs had only scurvy, as he characterizes his animals as having badly swollen joints and hemorrhages of the gums. These symptoms in the experience that I have had with some 150 scorbutic guinea-pigs during the past year and a half do not seem to me to be characteristic enough to permit a diagnosis of scurvy. It has been my experience, both in guinea-pigs fed according to the direction of Holst and Fröhlich<sup>27</sup> on the one hand and Jackson and Moore<sup>29</sup> on the other, that the animals fail to show what I should wish to call hemorrhages of the gums. This experience coincides with that of Holst and Fröhlich,<sup>27</sup> who did not find in their pigs hemorrhages of the gums as we see them in the human being. They did find, however, that the molar teeth became loose and were readily extracted. It seems to me probable that the beneficial results which McCollum and Pitz obtained by liberally dosing their guinea-pigs with liquid petrolatum will more readily fit into the clinical, therapeutic and pathogenetic picture of rickets or pseudo-rickets, as we know them at the present moment, than of scurvy. As Hart<sup>15 16 17</sup> states, it is impossible to know without a microscopic examination of the bone whether in scurvy cases showing swellings that resemble those seen in rickets only one disease or both diseases are present. I think, however, that this statement of Hart's may in certain cases be modified by the roentgen rays. Aside from McCollum and Pitz and Jackson and Moore, most men, such as Funk,<sup>11 12</sup> Vedder,<sup>52</sup> Braddon and Cooper,<sup>3</sup> Holst and Fröhlich,<sup>27</sup> Schaumann,<sup>47</sup> Hart,<sup>15 16 17</sup> Hess,<sup>19 22</sup> Fröhlich,<sup>10</sup> Fürst,<sup>14</sup> Budd and

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Busk,<sup>14</sup> and others, are of the opinion that the disease is a "deficiency" disease, due to an absence or inaction of one of the so-called "vitamines," "accessory growth factors," or one of the known food constituents.<sup>43</sup>

II. CLINICAL PICTURE. The clinical picture of scurvy has been controlled until recently by two symptoms, namely, hemorrhages into the bones and tissues and rarefaction and swelling of the osseous system. In 1914 Darling,<sup>8</sup> however, in his articles on "The Pathological Affinities of Beriberi and Scurvy," called attention to the distinct similarity between scurvy and beriberi in the production of some symptoms. He pointed out the presence in scurvy of exaggerated reflexes, tachycardia and dilatation of the heart. On microscopic examination he found fatty degeneration of the heart muscles and also degeneration of the vagus, while the other heart nerves were free from any lesion whatsoever. According to Lesage,<sup>33</sup> he and various other French authors as early as 1906-8 recognized the hyperesthetic form of scurvy which at times was clinically negative in every other respect and was diagnosed by its prompt response to antiscorbutic treatment. At the beginning of this year Hess<sup>22</sup> reported similar findings. So at the present time we have, from a clinical stand-point, symptoms that are referable to changes in the bloodvessels, in the osseous system, the nervous system, and the muscular system.

III. PATHOGENESIS. Hart<sup>15 16 17</sup> states that while on the one hand there is no doubt as to scurvy being a disease *sui generis*, yet there is, on the other hand, no settled opinion as to whether one and the same agent or process is responsible for the changes in the bones and the bloodvessels or whether they are due to different agents or whether they are interdependent upon each other. But it has seemed to me, in view of the known data regarding the pathology, chemistry and symptomatology of scurvy on the one hand, and regarding the important function played by calcium in bone growth, nerve conduction, vessel sealing, and cell permeability on the other, that all of these different system symptoms might be explained on the common basis of an interference with one or more of the normal functions of calcium and its physiological anion in the osseous system, vascular system, nervous system, muscular system and probably other systems.

So I have imagined the following:

1. That all of the symptoms of scurvy as we know them today may be explained on the common basis of a primary or secondary interference with one or more of the normal functions of calcium, alone or in conjunction with its physiological anion, a condition which I am pleased to call a *partial defunctioning of calcium and its physiological anion*. The work of Heubner<sup>24</sup> and Lipschütz,<sup>34</sup> namely, shows that for the ascorbutic development of the osseous system the presence of phosphorus in sufficient quantity is necessary.

2. That in scurvy as we see it occur in infants this defunctioning is caused by a substance produced through a break in the metabolism of carbohydrates, whatever their original source may be.<sup>52</sup>

3. That the break in carbohydrate metabolism occurs, as already suggested by Funk,<sup>12</sup> Braddon and Cooper<sup>3</sup> and others, as a result of the absence or inactivity or relative insufficiency or inadequacy or some physicochemical substance or "vitamine" essential to the establishment and performance of normal carbohydrate metabolism, possibly in the role of a catalyzer, as suggested by Schaumann,<sup>47</sup> as quoted by Holst and Fröhlich.<sup>27</sup>

4. That the defunctioning substance produced as a result of the break in the metabolism of carbohydrates due to a disproportionment between the carbohydrate supply on the one hand and the "vitamine" supply on the other, possibly is oxalic acid or some other agent that has a similarly strong affinity for calcium, and that after combining with calcium is soluble with similarly great difficulty.

There is, to my knowledge, no function whose perfect operation depends solely upon the presence and actions of only one and the same factor, and there is also, to my knowledge, no disease that is produced in every instance by the action of only one and the same factor.

A normal function can be pictured as an intact circle of links, and an abnormal function or disease has a circle of links broken in one or more of its links. Various and numerous circumstances and conditions will determine the link or links that usually break and produce a disease in a given environment, but occasionally in the same environment an entirely different link will break and, in consequence, just as successfully make impossible the performance of the same function in a normal manner and just as successfully develop the same disease, at least in its more important symptoms. Clinically the abnormal function may present itself to us in both instances in exactly the same picture, but it also is possible that the picture be different in some particulars while the same in others.

A good example of this in experimental scurvy has been given by the work of Heubner and Lipschütz referred to above. These authors fed dogs on a phosphorus-low diet and produced lesions, which, according to Schmorl,<sup>48 34 24</sup> are identical with the most characteristic lesions found in classically scorbutic bones, and yet the scorbutic bone lesions that we see in infants are often produced in a child on a diet whose phosphorus content is high rather than low, and in this latter instance, simply because, in all probability, for one reason or another, the phosphorus is prevented from performing its normal function in bone growth. This work of Lipschütz and Heubner, I believe, proves that phosphorus, at least so far as normal bone growth is concerned, is just as necessary as is calcium, and so I think that one can readily agree with the statement made by Masslow,<sup>41</sup> quoted by Baumann and Howard,<sup>2</sup> namely, that in the pathogenesis

of the disturbances of the osseous system phosphorus plays a distinct role. Whether phosphorus joins calcium in a similar fashion in the function of sealing vessels or conducting nerve impulses, so far as the clinical picture and lesions of scurvy are concerned, is another question which cannot be answered at this time.

In connection with the work of Heubner and Lipschütz it should be stated that Walter Löb<sup>39</sup> is of the opinion that the presence of phosphates is necessary for normal glycolysis. However, as the sick dogs of Heubner and Lipschütz gained decidedly in weight while they were producing their own lesions it would seem, to say the least, that even the small quantities present in the diets of the dogs were sufficient to meet the glycolytic phosphorus needs of their bodies.

That calcium, however, has a distinct function to perform in the sealing of vessels and nerve conduction there can be no question, as the work of many authors shows. Chiari<sup>5</sup> has proved that saline cathartics act by increasing the permeability of the vessel wall by binding with their calcium and so extracting it from them. In another study it was possible for him and Januschke,<sup>7</sup> by a protective injection of calcium, to prevent the formation of an exudate on the conjunctiva of a rabbit into whose eye a drop of mustard oil was dropped. Overton,<sup>46</sup> quoting Herbst, states that the sealing substance in the tissue cells of certain animals is loosened by the removal of calcium and tightened by the readministration of calcium, and Januschke<sup>36</sup> was able to prevent the appearance of the usual and characteristic pleural exudate in iodine poisoning in dogs by the giving of calcium. Sir A. E. Wright<sup>57</sup> also found that calcium could prevent the development of certain urticarias, and he was inclined to attribute this beneficial effect of the calcium to the increased coagulability of the blood produced by it. Chiari and Januschke<sup>7</sup> took up this point and proved that the vessel-sealing function of the calcium was not the same as the one it performed in the coagulation of the blood; in other words, that it could perform the one without performing the other. These authors proved this by injecting hirudin into a rabbit that had been pretreated with calcium. Two hours later mustard oil was dropped into the eye and no exudate resulted, even though the coagulation time of the blood was kept distinctly below normal by the hirudin.

Hess<sup>19</sup> has shown that infants with scurvy show on the one hand a practically normal coagulation time, and on the other an increased permeability of their vessel walls as tested by the capillary test. While, as Hess states, this test is not pathognomonic of scurvy, as it occurs in many other conditions, yet it seems to me that its apparently constant presence in a marked form in scurvy makes it speak for the existence of an increased permeability of the vessel walls in scurvy. Holst and Fröhlich<sup>27</sup> fed their guinea-pigs calcium in different forms without getting any beneficial effect. Likewise

Ingier<sup>28</sup> did not succeed in checking the development of the scorbutic phenomena in pregnant guinea-pigs by adding phosphorated cod-liver oil to the diet, and Hess<sup>19</sup> reports the same negative results with infants. I also have given large doses of cod-liver oil with tricalcium phosphate to a florid case of scurvy absolutely without any beneficial effect (5 c.c. of cod-liver oil containing 20 per cent. tricalcium phosphate, twice daily for eight days). So that it is clear that the lessened permeability of the vessel wall in scurvy is produced in a manner that, in some particular at least, is different from that operating in the experiments carried out by Chiari and Januschke<sup>5 7 31</sup> and others.<sup>32</sup> Nevertheless, it is true that the vessel walls in scurvy are more permeable than normal, and also that calcium plays an important part in sealing the vessels, and so, in view of the additional fact that a disturbance in the calcium metabolism exists in scurvy, it still would seem possible that somehow an interference with the vessel-sealing function of calcium is responsible for the increased permeability of the vessel walls in scorbutic infants.

Chiari and Fröhlich<sup>6</sup> have further demonstrated that the autonomic nervous system is stimulated by the removal of calcium. This removal of calcium was produced by oxalates, and Januschke<sup>31</sup> showed that calcium antagonized this action of oxalates. H. H. Meyer,<sup>45</sup> in a short address referring to the work of the just-mentioned authors, states, "Our experiments prove two things: (1) a sedative action of the calcium on the vegetative nerve apparatus, and (2) a lessening of the permeability of the vessel wall."

Burridge,<sup>4</sup> in his very important experiments "On the Localization of the Calcium and Potassium Salts Concerned in the Mediation of the Action of the Vagus Nerve on the Heart of the Frog," definitely has found that "calcium salts are essential to complete passage from the preganglionic nerve fibers to the heart ganglia and that potassium salts favor the action of the terminal structure concerned in vagus action." He also states that the calcium salts, mediating the action of the vagus nerve on the frog's heart, form an integral part of the structure, whatever it may be, on which the nicotin acts. He further quotes the work of Chiari and Fröhlich, Meyer and Januschke, mentioned above, and that of Elliot,<sup>4</sup> who pointed out certain analogies between the synapses of the autonomic nervous system and the nerve endings of skeletal muscles. So these experiments also prove not only that calcium has an important function to perform in the transmission of nerve impulses, but that its defunctioning can produce symptoms such as we see presented in the heart and in the nervous systems of patients ill with scurvy and beriberi. Finally, it is well to call attention to the extremely important work of Jacques Loeb<sup>35 36 37 38</sup> and his co-workers regarding the function of calcium and other salts in cell permeability and irritability. He has proved<sup>37</sup> for calcium that the two functions are not the same and that in order to perform one



certain conditions must be different than are present for the operation of the other.

None of the cases of scurvy that I personally have seen have shown a hyperexcitability to the galvanic current, and none of the cases of spasmophilia that I have tested have shown an increased permeability of their vessel walls, proving that while in each case there is a disturbance in the function of calcium, yet the clinical reaction to the same tests may be entirely different in each case. Of course, cases will be, or possibly have been, observed that show signs both of scurvy and spasmophilia.

Additional and important insight into the pathogenesis of the disease under discussion has been obtained by the observations of Lust and Kloeman<sup>40</sup> on the one hand and through those of Bahrdt and Edelstein<sup>1</sup> on the other. The former found in studying the metabolism of a marked case of scurvy in an infant that during the active stage of scurvy there was a retention of the minerals investigated by them, namely, calcium, phosphorus and chlorine, especially that of the calcium, and that during the convalescent period of the same case there was a negative balance produced by an excessive excretion of the same salts, and finally that in the stage of healing, while the total ash and phosphorus balances were positive, the calcium balance remained still negative. This discovery by Lust and Kloeman finds corroboration in the microscopic and roentgenologic study of scorbutic bones. As is well known, Hoffmann,<sup>26 40</sup> Schmorl,<sup>43 34</sup> and other pathologists have described the presence of an increase rather than a decrease of the preparatory zone of calcification. Hoffmann<sup>40 26</sup> even speaks of a calcium congestion, and Fränkel,<sup>9 40</sup> with the roentgen rays, first called attention to the presence of the more or less broad, white line at the junction of the epiphysis and diaphysis of the long bones, and showed that this line disappears extremely slowly and is, as a matter of fact, still present when otherwise from a clinical stand-point the child seems perfectly well.

Bahrdt and Edelstein,<sup>1</sup> however, in the chemical analysis of bones from a marked case of scurvy, made discoveries which at the first glance seem to contradict those of Lust and Kloeman.<sup>40</sup> Instead of showing an increase in the calcium and phosphorus content of the bones, as one might have expected from the findings of Lust and Kloeman, they found a distinct deficit in calcium and phosphorus of the bones and muscles, with an increase in the water-content and possibly also in that of sodium and potassium. They also believe that the sodium and potassium of the liver and kidney were somewhat decreased while the calcium content of these organs was normal if not above normal. These authors state that their findings would indicate that the kidney and the liver, on the one hand and the bones and muscle on the other, take opposite positions in the calcium metabolism. They are not so sure as to the application of this state-

ment to phosphorus, as it was found normal in all of the internal organs examined and also in the muscles.

Although the two findings of these two groups of authors seem to contradict each other, yet it seems to me perfectly possible that they do the opposite. The microscopic picture of scorbutic bones shows an increased deposition of calcium along the epiphyseal line but an increased porosity in the rest of the bone, especially in the diaphysis. This histological picture corresponds, as already stated above, with the roentgenologic, and I should think it perfectly plausible to assume that this condition is produced by a continuance of the normal function of bone resorption and a synchronous breaking-down of the normal function of bone development. That this latter in scurvy is not due to a deficiency in calcium is clearly proved by the microscopic picture and the roentgenological pictures which show an increase in the layer of calcification at Fränkel's line. In other words, while there is a certain amount of calcium being deposited at the part of the bone at which endochondral growth takes place under normal conditions, there is, nevertheless, in all probability not as much calcium in the whole bone at a certain advanced stage of scurvy as there would be in the normal, because in the first place the bone has ceased to grow either entirely<sup>20</sup> or at any rate not as markedly as under normal conditions, and in the second place the normal process of resorption is going on, producing a rarefaction and brittleness, with consequent loss of material. So it should be perfectly possible to find in the same child (1) an excess of calcium at the end of the bone in Fränkel's white line, (2) a reduction in the amount of calcium in the bone as a whole, such as Bahrtdt and Edelstein found, and (3) a positive calcium balance, such as Lust and Klocman found, if but one thing happens, namely, that for some reason or other a holding down of calcium occurs in other parts of the body besides in parts of the bones. That there can be such a retention is indicated by the experience of Lust and Klocman, and even by the findings of Bahrtdt and Edelstein themselves, who found a relative increase in the calcium content of the liver and kidney. An observation which I had occasion to make in a scorbutic child during June, 1916, also speaks in favor of a salt retention during the active stage of the disease. This child showed a marked difference between the water excretion by the kidney during the active and during the convalescent stages of the disease.

The chart below gives the details and shows that there was during the active stage a marked reduction in the amount of water excreted by the kidneys, which was not accompanied by a net increase in weight or by any significant change in the stools. Neither was there an influential change from the normal in the temperature chart, and the outside temperature was distinctly lower than it was during the stage when orange juice was given. The giving of orange juice markedly increased the urinary output

TABLE SHOWING URINE EXCRETION, ETC., DURING SCURVY.

Date, 1916.	Mean daily temperature.	Mean daily relative humidity.	Mean daily relative humidity.	Drugs.	Total fluid intake in 24 hours, including O. J. when given, c.c.	Average daily group intake, c.c.	Urinary output in twenty-four hours, c.c.	Average daily group output, c.c.	Average daily urinary output, per cent.	Average daily group output, per cent.	Stools.	Body temperature.	Body weight grams.
June 22	60	61	61	None	1000		265		20.5		1 N	36.8-37.0-36.8	6570
23	64	56	56	"	720		65		9.0		1 E	30.9-36.8-37.1	6610
24	72	60	60	"	520		69		13.2		1 N, 1 sl. thin	37.4-38.2-37.2	6600
25	66	59	59	"	580	751.3	190		19.3	20.9	1 N, 2 N	36.8-37.1-36.5	6660
26	69	58	58	"	422		26	107.2	6.1		1 N	36.5-37.1-36.5	6590
27	65	83	83	"	740		145		19.5		1 N	37.0-37.2-37.0	6370
28	62	80	80	"	700		355		40.7		1 N, 1 choppy	37.0-37.4-37.0	6410
29	66	68	68	"	700		202		26.9		1 N	30.5-37.5-37.0	6480
30	68	60	60	"	800		183		21.3		1 N	30.5-37.4-37.4	6530
July 5	70	70	70	"	480	400.0	11	13.5	2.3	13.03	1 N	37.3-37.9-37.0	6350
6	68	58	58	"	320		80		25.0		2 N	37.3-37.8-37.5	6300
7	70	52	52	Pot. cit. 1x1 gm.	680		128		23.0		1 N	37.3-37.5-37.0	6260
8	72	70	70	"	620	530.0	89	149.7	11.1	26.35	2 N	37.5-38.0-37.4	6220
9	68	78	78	"	620		203		32.7		0	37.0-37.4-37.3	6250
10	72	70	70	"	500		180		36.0		2 choppy	37.3-38.3-37.5	6180
11-13	..	..	..	None	....		...		....		On the 11th:	37.3-38.8-38.8	6270
14	77	72	72	Na cit. 4x1 gm.	400		65		16.2		2 N	37.4-37.2-37.2	6200
15	81	64	64	"	470		200		42.5		0	37.7-37.7-37.3	6270
16	74	78	78	"	640		210		32.8		1 N	37.0-37.0-37.0	6230
17	75	80	80	"	410	512.8	175	108.5	30.7	31.1	2 N	36.8-37.3-37.3	6230
18	78	88	88	"	600		255		42.5		0	37.3-37.3-37.1	6090
19	80	77	77	"	530		100		30.1		1 choppy	37.3-37.2-37.1	6160
20	78	90	90	"	720		115		15.9		1	36.0-30.9-37.1	6160
21	70	68	68	Or. " Orange juice	?		420		47.1		...	36.8-37.4-37.9	6130
22	74	64	64	O. J. 60 c.c.	520		245		37.9		1 N	37.5-37.2-37.2	6080
23	70	59	59	" 90 "	970		310		41.9		1	37.2-37.3-37.3	6060
24	77	56	56	" 90 "	960	835.0	345	320.0	32.5	40.15	1	39.3-37.5-37.0	6090
25	78	68	68	" 90 "	1030		335		32.5		1	36.9-37.1-37.0	6160
26	78	68	68	" 90 "	1020		415		40.0		1	37.0-37.3-37.3	6260
27	80	62	62	" 90 "	510		270		53.9		1		

from 20 per cent. of the intake to 40 per cent., even though at this time the outside temperature was distinctly higher (14.1° F.). And in the face of this increased urinary excretion the infant made a net gain in weight, showing, just as the general appearance of the infant did, that the body was again working in a more normal fashion. Surely the simplest interpretation that can be given to this observation of decreased water output by the kidneys is a retention of salts by the body, either as a protective measure or simply as a result of hindered salt excretion, and that the water was given off mainly by way of the lungs.

This finding seems especially significant in view of the fact, as can be seen from the chart, that the giving of potassium citrate had only a little effect upon the urinary excretion. The amount of urine passed within twenty-four hours, however, notwithstanding the increase in outside temperature, was somewhat more increased by the giving of large doses of sodium citrate, and both in this case and in another it was observed that there also was a distinct but temporary improvement in the general condition of the scorbutic child after the administration of this salt; so marked was this in the one instance that the gums became distinctly reduced and pale, only, however, to get worse again in the face of the continued administration of the drug. The general behavior of the child improved within twenty-four hours, the gums were pale and decidedly reduced after 3 x 24 hours, and after remaining so for an additional 2 x 24 hours became abruptly worse again without any change in the therapy having been instituted in the meantime.

This same decrease in urinary excretion in the water output by the kidneys seems to occur in guinea-pigs getting scurvy on a diet of oats and water, for frequently I find in my notes the observation recorded that the sawdust pens of these animals at about the second week of the disease were especially dry and clean, and since having made the above-described observation in the infant with scurvy I have had occasion to ask four mothers of scorbutic infants regarding this symptom, and they all state that the baby "did not wet nearly as much since it had been sick as it did when it was still well." If this observation is confirmed and found to be present in most cases of infantile scurvy it will represent an addition to the clinical symptomatology of scurvy.\*

Very recently Bauman and Howard<sup>2</sup> in their study of the mineral metabolism of normal and scorbutic guinea-pigs, reported findings which are in contradiction to those reported by Lust and Klocman

\* Since this article was presented, A. F. Hess (*Infantile Scurvy: V. A Study of Its Pathogenesis*, *Am. Jour. Dis. Child.*, 1917, xiv, 337) has expressed the opinion that the increased pouring out of water by the kidneys after the administration of orange juice was due to a simple diuretic effect of the orange juice. However, from the experience obtained in this case with the administration of large doses of potassium citrate, which is the classical diuretic and much more effective than sodium citrate, it would hardly seem that Hess's interpretation were correct.

for their infant. They found, namely, that all of the elements, except magnesium and chlorine, showed a negative balance during the scurvy period.

There can be no question that clinical experience with infantile scurvy points strongly to the carbohydrate high foods, everything else being equal, as being the most prominent factors concerned in the production of the disease. As already stated, Funk<sup>12</sup> and Braddon and Cooper<sup>3</sup>—the latter for beriberi—believe that the greater the amount of carbohydrate content of the food the greater will be the amount of "vitamine" required to keep up a normal carbohydrate metabolism, and the sooner the body supply of "vitamines" will be exhausted, especially if by various means, principally by heating, the "vitamines" present in any food are made useless.

At the time when Braddon and Cooper's<sup>37</sup> article appeared I had occasion to see a thirteen-months-old infant in a state of malnutrition and ill with a distinct clinical scurvy. This infant had been fed on various kinds of foods since its second month, but during the three months previous to his coming to me he had received, according to the mother, nothing but raw milk diluted with water, together with enormous amounts of Mellin's Food (sixteen heaping table-spoons). I questioned the mother carefully as to the manner in which she had warmed the bottle and how she had prepared the milk, but could only come to the conclusion that she had not warmed the bottle differently than is desirable. This made me feel at the time that this infant represented a counterpart to Braddon and Cooper's pigeons, and I still think so.

In this connection the experiments of Mayer<sup>12</sup> and Hildebrandt<sup>25</sup> are very suggestive, as these authors were able to prove a breaking down in the oxidation process of sugar in animals after having administered excessive doses of carbohydrates. And what is more, they have proved that under these circumstances at least a certain part of the oxidation of glucose stops with the production of oxalic acid, an acid which, as is well known, has an enormous affinity for calcium and with it forms a salt that is soluble with great difficulty.

However, all of the symptoms produced by these authors and others, such as Chiari, Chiari and Fröhlich, and Januschke,<sup>5 6 7 31</sup> by binding calcium through the administration of oxalic acid could be prevented or, at any rate, modified and lessened by giving calcium in sufficiently large doses, an experience that has not been met with in cases of scurvy that have received calcium and cod-liver oil in seemingly adequate doses—Hess,<sup>19</sup> Ingier,<sup>23</sup> and H. J. G. (see page 257). And then, as Sedgwick has shown, newborn infants excrete within twenty-four hours a much larger amount of oxalic acid than do adults, and give evidence of no condition that can be compared with any of the known symptoms of scurvy.

So that while there are many clinical and experimental data that seem to speak strongly against the assumption that oxalic acid is

responsible for the defunctioning of calcium and its corresponding physiological anion, it has nevertheless seemed worth while to me to try to settle this question by resorting to every means possible to try to find oxalic acid present in cases of scurvy as a calcium fixer, because not only would its presence explain the production of the various symptoms described in the earlier part of the paper as a result of defunctioning calcium and its physiological anion in the bones, the vessels and the nervous system, etc., but also the rapid and marvelous disappearance of the symptoms just mentioned by the oxidation of oxalic acid in the presence of the physicochemical substance or "vitamin" necessary for normal and complete oxidation of carbohydrates and through its consequent primary release of calcium and its secondary release of other salts.

And it seems to me, in the face of the adverse experimental data mentioned above, as if, after all, oxalic acid could be responsible for the defunctioning of calcium and its physiological anion, if we assume that the production of the oxalic acid and its binding with calcium occurs within certain cells themselves, or in tissues that are poorly supplied with blood and lymph vessels, such as cartilage, both places where the solution of a salt like calcium oxalate would be distinctly less readily accomplished than, for instance, in the blood stream itself.

That the conditions for salt solubility in a given tissue system or, in other words, its fluid inflow and outflow, and the extensiveness of the system also may be a factor of decided importance in the production of the type and behavior of the different clinical, histological and chemical symptoms of scurvy, seems probable from a consideration of the location of the lesions in the vessels and in the bones.

It is certain that the most marked changes occur where bone growth is relatively greatest and where at the same time the blood supply is relatively smallest. So in the lower extremities the more severe lesions are located in the neighborhood of the knee, and in the upper extremity in the neighborhood of the wrists and shoulders, all parts of the extremities lying in the opposite direction of the nutrient artery. Then, the lesions limited to the vessels all clear up much more rapidly than those occurring in the bone, and in the bone again the lesions last to disappear are those in the region of Fränkel's white line, surely a part of the bone which has less blood-vessels than that near the periosteum, a fact that also can well explain why Fränkel's line persists much longer than any other one symptom of scurvy.

From the close dependence of the severity of the vessel lesion on its proximity to growing bone, one might believe that the substance which defunctionates calcium and its physiological anion is produced solely by the bone cells, the osteoblasts, and that the vessel lesions are produced by the vessel cells coming into contact

with this agent during its passage in the blood stream. But the published accounts of hyperesthetic cases such as were described by Lesage<sup>33</sup> and of cases showing hematuria as the only symptom, make it more probable that cells of different systems may not be able to entirely oxidize carbohydrates in a normal manner. It also may be possible that the hematuria may be produced as a result of a change in the chemical form of the attacking agent during its excretion by the kidneys, although this does not seem plausible for other reasons. So taken all in all it does seem as if various cells, some for hereditary and some for acquired reasons, first break down and more completely than other cells in the performance of their carbohydrate metabolism and consequently show clinically recognizable signs of scurvy, either alone or in advance of cells located elsewhere. That, however, all vessel lesions in their entirety are not due solely to the breakdown of the carbohydrate metabolism of their own cells, would seem to be true from the close connection existing between the severity of the bloodvessel lesions on the one hand and of their proximity to the bones on the other. This is most beautifully demonstrated by the lesions occurring in the gums only when the teeth are erupting or have erupted; in other words, at a time when the alveolar periosteum is very active and when the gums have become firmly attached at the neck of the tooth to the tooth and to the periosteum.

Also periosteal bone formation is a much more vascular process than endochondral bone formation is, and this further explains the presence of the greatest hemorrhagic lesions along the periosteum.

At the present moment, however, I do not find myself in a position definitely to state that oxalic acid is or is not the defuncting agent responsible for the production of the clinical symptoms of scurvy, even though I have diligently and persistently tried to prove its presence for more than twelve months. However, I expect to be able to report within the very near future.

It may be that another substance may be responsible for the clinical symptoms of this disease, but if this is so then it seems to me as if it must have the same powers regarding the defuncting of calcium and its physiological anion that oxalic acid has, and the same *modus operandi*.

It is also possible that the defuncting of calcium and its physiological anion does not occur through the action of the kind of substance indicated above or within the cell, or solely within the cell, but that it occurs in the cell membrane, at least partly so, and there, *via* the same or another *modus operandi*, affects the cell permeability in a manner as suggested by the interesting and important experiments of Jacques Loeb.<sup>35 36 37 38</sup> The observation made in the two scorbutic infants after the administration of sodium citrate might be interpreted in this manner.

Observations made by me in experimental work with a scorbutic infant and with pigeons ill with polyneuritis\* make me feel that in all probability we shall find that the defunctioning agent is produced as a result of a broken-down carbohydrate metabolism due to a disproportionment within the cells between the carbohydrate supply on the one hand and the physicochemical substance, the so-called "vitamine," growth factor or known substance on the other.

These observations have shown that there is an immediate, distinct and marvelous change produced in the pigeons ill with polyneuritis by the administration of yeast, and in the scorbutic child by the administration of orange juice in the respiratory quotient† that can only be interpreted as indicating an immediate and marked rearrangement and readjustment in some known or unknown oxidative process of the body.

This observation is an added argument against the assumption of McCollum and Pitz,<sup>44</sup> that scurvy is produced in guinea-pigs as a result of constipation. Before any orange juice can possibly get down to the large intestines a definite and distinct change can be registered by the respiratory apparatus. And then constipation is not a part of the clinical picture of scurvy, as it does not occur with any kind of regularity or frequency in scorbutic infants, and the large intestine of my scorbutic guinea-pigs on oat-and-water diets have off and on been practically empty at necropsy.

The remarks regarding the observations obtained by studying the respiratory quotient in the scorbutic infant and in polyneuritic pigeons are also to be considered as having been made in the sense of a preliminary statement.

RÉSUMÉ. 1. An hypothesis is offered regarding the pathogenesis of infantile scurvy.

2. The hypothesis is divided into four separate parts, of which only the first is considered to be sufficiently based on experimental and clinical data to permit its exit out of the domain of pure hypothesis.

The second and third, the latter of which has been similarly and previously advanced by other authors, are considered to have as a basis experimental and clinical data that are distinctly suggestive, while the fourth is still purely hypothetical, although on its assumption it is possible to explain satisfactorily some of the clinical phenomena of scurvy that hitherto have had not even an hypothetical explanation.

\* Very suggestive data can be found in the work reported by MacArthur and Jones (Some Factors Influencing the Respiration of Ground Nervous Tissue, *Jour. Biol. Chem.*, 1917, xxxii, 271), who studied the respiratory quotient of different parts of the central nervous system and found that the respiratory quotient is higher in white matter than in gray, and higher in the peripheral nerves than in the other portions of the nervous system.

† Ibid.



3. A report is made of a case of infantile scurvy which showed a marked reduction in the water output of the body through the kidneys without the presence of the usual and known causes for water loss *via* other channels, and which further showed a marked change toward a return to normal conditions by the administration of orange juice, indicating a protective salt retention or hindered salt excretion as the cause of the transfer of a good portion of the water excretion from the kidneys to the lungs.

The same condition seemingly was present in 4 additional cases of infantile scurvy as well as in scorbutic guinea-pigs on an oat-and-water diet.

It is suggested that the phenomenon observed is a part of the regular picture of infantile scurvy and represents an addition to the clinical symptomatology of scurvy.

4. A case of infantile scurvy is reported as being a counterpart to Braddon and Cooper's polyneuritic pigeons by having developed its symptoms on a diet of raw milk, modified, however, by dilution with water to one-half and by the addition of enormous amounts of carbohydrates in the form of Mellin's Food.

5. The experience of other authors regarding the inefficiency of cod-liver therapy and calcium therapy in scurvy is corroborated by absolutely negative therapeutic results having been obtained in a case of infantile scurvy upon the administration of tricalcium phosphate and cod-liver oil, indicating that a deficiency of calcium in the diet or in the body plays no primary role in the development of scurvy.

6. A report is made of a distinct but temporary improvement in the clinical picture of 2 cases of infantile scurvy upon the administration of large doses of sodium citrate. This observation suggests the possibility of the existence in the development of the clinical picture of infantile scurvy of a *modus operandi* similar to such as has been shown to exist in cell permeability and irritability by the researches of Jacques Loeb.

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# WAR MEDICINE

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- MAJOR E. G. BRACKETT, M.R.C., U.S.A. (Assistant Prof. of Orthopedic Surgery, Harvard Medical School).
- MAJOR R. M. YERKES, Sanitary Corps, U. S. A. (Prof. of Psychology, Harvard University).
- SURGEON M. J. ROSENAU, U.S.N.R.F. (Prof. of Preventive Medicine and Hygiene, Harvard Medical School).
- MAJOR R. TAIT MCKENZIE, R.A.M.C. (Prof. of Physical Therapeutics, Univ. of Penna.).
- MR. DOUGLAS C. MCMURTRIE, Director of Red Cross Institute for Crippled and Disabled Men, New York.
- DR. E. E. SOUTHARD, Director of Psychopathic Department, Boston State Hospital.
- MAJOR WARFIELD T. LONGCOPE, M.R.C., U. S. A. (Prof. Practice of Medicine, Columbia University).
- DR. C. V. CHAPIN, Superintendent of Health, Providence, R. I.
- DR. GRACE L. MEIGS, Children's Bureau, U. S. Department of Labor.
- DR. A. N. RICHARDS, Professor of Pharmacy, Univ. of Penna.
- DR. W. H. F. ADDISON, Assistant Professor of Histology, Univ. of Penna.
- DR. DAVID L. EDSALL, Professor of Clinical Medicine, Harvard Medical School.
- DR. GRAHAM LUSK, Professor of Physiology, Cornell Medical School.
- DR. O. H. PERRY PEPPER, Associate in Medicine, Univ. of Penna.
- DR. W. P. LUCAS, American Red Cross (Prof. of Pediatrics, Univ. of California).
- MAJOR FRED H. ALBEE, M.R.C., Director of Military Reconstruction Hospital No. 3, U. S. A.
- DR. RUFUS COLE, Director Rockefeller Hospital.
- LIEUTENANT E. ESTELL LEE, M.R.C., U. S. A.
- DR. JOHN A. HARTWELL, Assist. Prof. of Surgery and Prof. Clinical Surgery, Cornell Medical School.
- DR. RALPH PEMBERTON, American Red Cross.
- DR. DOROTHY REED MENDENHALL, Children's Bureau, U. S. Department, of Labor.
- ASSISTANT SURGEON PAUL A. LEWIS, U.S.N.R.F. (Pathologist to Phipps Institute, Philadelphia).

## THE WORK OF THE CHILDREN'S BUREAU, DEPARTMENT OF CIVIL AFFAIRS, AMERICAN RED CROSS, FRANCE.

By WILLIAM PALMER LUCAS, M.D.,<sup>1</sup>

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### I.—THE SITUATION IN AUGUST, 1917.

THE children's situation in France as we found it on our arrival in August was somewhat as follows:

France had been at war for three years. Practically all her men of fighting age were at the front occupied in some branch of

<sup>1</sup> On leave by courtesy of the University of California as Chief of the Children's Bureau of the American Red Cross in France.

the Army or in the work of providing for the Army, so that most of the institutions which had been built up in times of peace for the care of children had suffered materially. Indeed, French children, as a whole, had not had the attention they received before the war. This condition is only too evident to one who makes a close survey of the situation, and the reasons for it are patent.

Here, as in Belgium, the main efforts for child welfare have been those dealing with infancy, so that where we did find any work established for children in France it was designed to increase the amount of nursing and care given to young infants. This work cannot be overestimated. It is the foundation stone; but the older child, especially the adolescent child, had received comparatively little attention. Under the circumstances this is almost inevitable. But here, as in Belgium, the absolute necessity of bridging such a gap was apparent if the efforts in behalf of the infants were to bear lasting fruit.

French children, as a mass, are underfed, undernourished and insufficiently clothed, especially those whose parents have been unable to provide for them out of means accumulated before the war. Probably at no time in the history of the world has there been such a widespread condition of underfeeding and poor nutrition as now exists in a very large proportion of French children.

Owing largely to the almost static condition of the civilian population there have been very few widespread epidemics: dangers of such epidemics increase with the moving about of refugees. If a widespread epidemic should occur at the present time I believe that the mortality would be very high, for the children have undoubtedly less power of resistance than they have ever had before. The infant mortality rates rose during the first year of the war, fell sharply during the second year, and began to rise again during the third year. There has been a very widespread increase in syphilis and venereal disease as a whole. In conjunction with certain economic causes these diseases have produced an increase in prematurity and in miscarriages.

Other social conditions exist, such as marked increase in juvenile delinquency and child labor, which have a direct relation to the health conditions among the children. These conditions, however, have such widespread economic significance that they must be treated separately. Here they are mentioned only in their relation to the health conditions. But it can be said of this situation here, as at home, that the breaking down of the normal individual home has an almost immediate effect upon the health conditions. These statements apply in varying degrees to most of the children of France. The task of social and medical effort which they present is enormous.

These general health conditions in France present some of the

gravest problems among the civilian population, and the Children's Bureau whose chief aim was medical care and conservation of the children, naturally took its place in the department of Civil Affairs of the American Red Cross. This Department, under Mr. Homer Folks, consists of a number of bureaus dealing with different civilian problems, such as Rehabilitation, Reconstruction, Housing of Refugees, Tuberculosis, and Children's Medical Work. The Children's Bureau immediately felt that not only was the closest coöperation with the French medical men and the French Government essential, but also that the closest coöperation between the different bureaus was absolutely necessary to meet the present health problem. From the first the Tuberculosis Bureau of the Red Cross, the Rockefeller Commission under Dr. Livingston Farrand and the Children's Bureau have worked in closest harmony. The medical problems, along general as well as special lines, as they appear in all bureaus dealing with the civil population in France, demanded, for effective work, the organization of a central medical committee. This committee, resulting as it has from the natural outgrowth of conditions, is able to simplify and unify the medical work among civilians. It was quite possible to be a tuberculous refugee child, sick with scarlet fever, and find the issue quite confused by the fact that three bureaus dealt with you. The present central medical committee, composed of (1) Dr. Miller, as chairman, representing the Rockefeller Commission, (2) Dr. White, Chief of the Tuberculosis Bureau, Red Cross, (3) Dr. Lucas, Chief of the Children's Bureau, Red Cross, (4) Dr. J. H. Mason Knox, Associate Chief of the Children's Bureau, and (5) Dr. Richard Cabot, of the Bureau of Refugees, strengthens and regularizes a coöperative interchange of medical aid which broadens and deepens the medical service which the American Red Cross can render the French in this hour of their great need. Civilian relief in France is largely a health problem, and it is along health lines that the approach is most quickly and tactfully made. The sympathetic understanding of this point of view by Mr. Homer Folks, the Director of the Department of Civil Affairs, is rendering the work of this Medical Committee more effective, and in all our public health undertakings the big, sane vision of Dr. Livingston Farrand, head of the Rockefeller Commission, is a constant source of help and inspiration.

## II.—WORK IN THE "ZONE DES ARMEES."

The most urgent need which faced us at the outset in August was that of the children from devastated areas in what is known as the "Zone des Armees," an area extending back for about thirty

miles from the front lines of the army. In this area we found towns which are likely to be bombed at any time, other towns partly destroyed, which had been evacuated early this year, and still others which were then being gassed, or were under continual shell fire. From this area the children are constantly being sent back in varying numbers; sometimes they are moved for short periods only during acute bombardment. At other times when the sector is suffering from more or less constant shell-fire or gas attacks the children have been evacuated more permanently. Here the problem is an urgent one. We have attempted to meet it in several towns which seemed to demand immediate attention and from which calls had already come to the Red Cross.

The largest undertaking of this kind has been in the Meurthe-et-Moselle Department under the kind guidance and auspices of Prefect Mirman. At his invitation the Red Cross has established a large clearing house and hospital at Toul. Here some 450 children and 50 mothers from gassed or bombed villages are housed and medically supervised. A women's and children's hospital for the whole Meurthe-et-Moselle Department has been started here, and its equipment largely given by the American Fund for French Wounded. Dr. Julius Parker Sedgwick, professor of pediatrics of the University of Minnesota, was the first director of this work in the Meurthe-et-Moselle, and it is due to his untiring patience and strength that the first three months of difficult pioneer work were brought to a successful establishment of the beginnings of what promises to be of such great service to the whole district. Dr. Sedgwick was most ably assisted by Dr. J. O. Durand, of Seattle, Oregon; Dr. N. O. Pearce, of Minneapolis, was also associated with the work at Toul. Upon the return of these doctors early in December to their university work at home, Dr. Maynard Ladd, of the pediatric faculty of Harvard University, assisted by Dr. Karlton Percy and Dr. Robert Sharp, also of the Harvard medical faculty, was appointed director of the Children's Work in the Meurthe-et-Moselle. Dr. Ladd is devoting himself to the further development of new centers in the district on the same plan as Toul. Prefect Mirman gives always his most splendid help and coöperation; indeed, his vision for the people of his department and his wise plans for them are a constant source of inspiration and strength to the American workers.

From the Hospital at Toul a biweekly dispensary service has been established in the factories and mairies of six nearby towns. This service is covered by Dr. Alice Barlow Brown, of Chicago, one of the American Fund for French Wounded medical delegates assigned by the bureau to the work in the Meurthe-et-Moselle under Dr. Ladd. This fund has worked hand-in-hand with the Red Cross for the realization of the great opportunities for service.

At these dispensaries groups of children and women ranging from a few hundreds in one town to over 1000 in another are cared for medically. This work is very urgent and impelling; to a certain extent the workers are in constant danger, since they are well within range of air raids or of the enemy's guns.

In this area the need is not only for the care of children but also for the care of women, and although the efforts of the Chil-

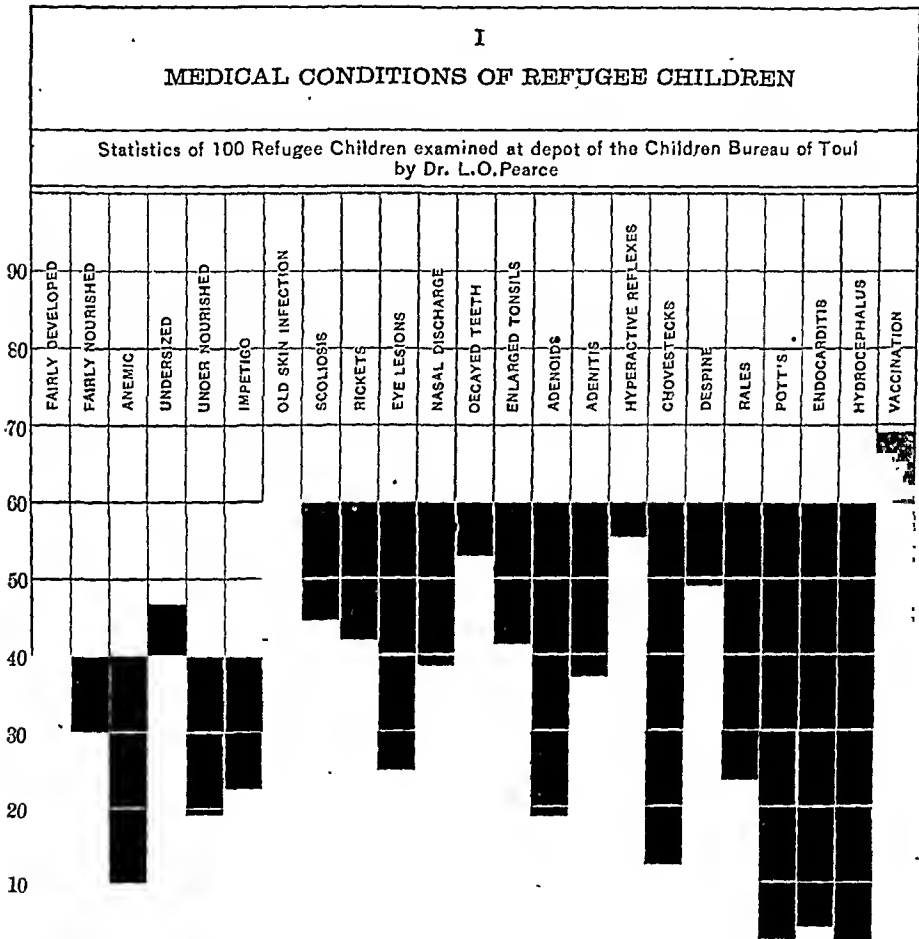


CHART I.—Chart of first 100 children examined at the hospital by Dr. N. O. Pearce.

dren's Bureau were planned at first wholly for the care of children, until the organization of the central Medical Committee, many adults had to be cared for. We have now at this station one physician specially trained for the care of women, so that obstetrical and gynecological cases will be admitted. In our dispensary work general medical diseases in adults had to be taken care of as the need arose, for it must be understood that most of the civilian population in the Zone des Armees has to rely for medical care



upon the doctors of the French military stations. Yet the physicians in these stations cannot always care for the civilian population adequately because the military exigencies of their own districts often demand their whole time for a long period. At these times the civil population must suffer. Hence we soon felt the need for a coöperation in our small health centers for children to include the care of the adult civilian population, and this need is now making itself felt more and more strongly throughout the Zone des Armees.

We have started another and smaller station with one doctor, two nurses, and an aid in a sector evacuated last spring by the Germans. Here we have organized a small hospital and a traveling dispensary to visit the small villages which have been devastated by the retreating Germany army, and are now being gradually reoccupied by their former inhabitants. Here the problems are manifold. The civilian population, as a whole, is helping to rebuild the houses; to reestablish workers in their trade, and to build up normal life in the devastated villages. The Children's Bureau is helping to solve the medical problem. This hard, rough, pioneer work has been done by Dr. John C. Baldwin, of Johns Hopkins University, with two nurses and an aide. To establish the little ten-bed hospital in a town full of ruined buildings meant days of scrubbing, cleaning, trucking, carrying of water and coal, the hardest kind of physical labor under most difficult living conditions. Patience, tact, kindness, coöperation, every human resource was brought into full play, and when the little wards were ready for the first cases of sick children the doctor wrote in his weekly report: "The need is so great, the people are so thankful, this first little child is worth the whole effort."

The need for such medical stations for the civilian population in the Zone des Armees is pressing and immediate. To meet it a number of American doctors, both men and women, have already responded to our call. Before very long we expect to have a competent working force sufficient to meet the greatest needs as they arise. In many cases we hope to establish small stations, with one doctor and perhaps two or three nurses; in other places larger stations may be developed. But it is very difficult, while military operations are going on at the present rate, to form any definite program. The Children's Bureau will try to meet each situation as it arises.

### III.—WORK FOR THE "RAPATRIÉS."

Another task which faced the Children's Bureau on its arrival in France was that of caring for the "rapatriés" as they enter France through Switzerland. At the present time the station of

entry is on the Lake of Geneva, in the small town of Evian, which has less than 5000 inhabitants. Into this town 1500 rapatriés pour each day, 750 in the morning and 750 at night. The proportion of children among them is from 40 to 60 per cent. of the whole number, so we have the task of caring for from 600 to 900 children a day. The largest number of children in any one convoy so far has been 680 Belgian children returning after three years of German subjugation. Anyone who saw these children, their emaciated, pitiful bodies, would realize how great a task confronted us at that point. It has been most difficult to secure adequate medical inspection of these children who came in by hundreds each day and were scattered throughout France the next day. If one visualizes this situation it is clear that the newly arrived children must be sent out of the city each day if the next 1500 rapatriés are to be cared for on the following day. The French needed and asked for help, with this problem, from the Children's Bureau.

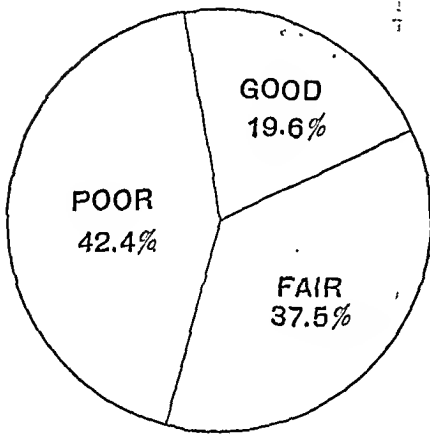
We have now established a system for the rapid inspection of every child so that we can weed out those who appear diseased and put them aside for a more careful medical examination. We have also established a hospital, accommodating from 80 to 100 children. Our staff of doctors there is now adequate. Dr. Edmund J. Labbe, of Portland, Oregon, is the chief of the hospital, with Dr. Clain F. Gelston, of the University of California, as first assistant. The dispensary examines on an average 2600 children per week. The hospital is always full. The contagious villa has been full from the start, cases of diphtheria, scarlet fever and measles coming in every convoy.

We have before us, at Evian, one of the most interesting problems in public health that has ever been presented in the field of children's medical and welfare work. It is like the medical problem of Ellis Island on a large scale, although, in other ways, it has no such parallel because these "rapatriés" are French people returning to free France from captive towns. The Germans are returning them to France simply to avoid caring for those of the civil population unfit to work in field, factory or trench, and that means largely old people and little children. We are dealing with children, but we also face the needs of adults, which the Children's Bureau does not attempt to meet. We are preventing the entrance of infectious diseases; we are weeding out the children suffering from chronic diseases, mostly tuberculosis; we are placing the underfed and undernourished but otherwise healthy children in convalescent homes, where they can be cared for, for periods long enough to bring their vitality up to a point somewhere near par before they are distributed into various parts of France, where they will be forced to remain until the war ends, or until their home towns are reconquered by the Allied Armies. Thanks to the present



distributed throughout France. Of these there are at present about 800,000, gathered in larger or smaller groups, sometimes as many as 10,000 in one place. In such centers we are building up health clinics in conjunction with the Department of the Red Cross dealing with the problem of medical relief for all refugees under Dr. Richard Cabot. Here, as in the Zone des Armees, the tasks are those of general medicine, although the greatest needs are those of the children and the women. There is very little obstetric work, because of the total absence of men under fifty years. These groups of refugees are composed mostly of old people, a moderate number of women in the child-bearing period, many children between three and fourteen years, but very few children above or below these ages. In these centers for refugees our work is one of careful medical examination, leading to the selection of those most in need of medical attention.

DEVELOPMENT



NOURISHMENT



CHART III

#### IV.—DISPENSARY SERVICE.

The fourth demand that the Children's Bureau is attempting to meet is in the dispensary situation in Paris. At each dispensary established by the Rockefeller Commission for Tuberculosis, under Dr. James Miller of New York, the Children's Bureau is coöperating in developing a Children's Department. At present two such centers are started, and Dr. John Manning, of Seattle, is in charge of the bureau's work in these two dispensaries.

Two dispensaries for general children's work have been established by the bureau in two of the most crowded sections of Paris. These have been started at the request of French physicians, who find the pressure tremendous. The city hospitals in these districts are

overcrowded and understaffed, and men like Dr. Marfan, of the Infant Malade Hospital, and Dr. Guinon, of the Bretonneau Hos-

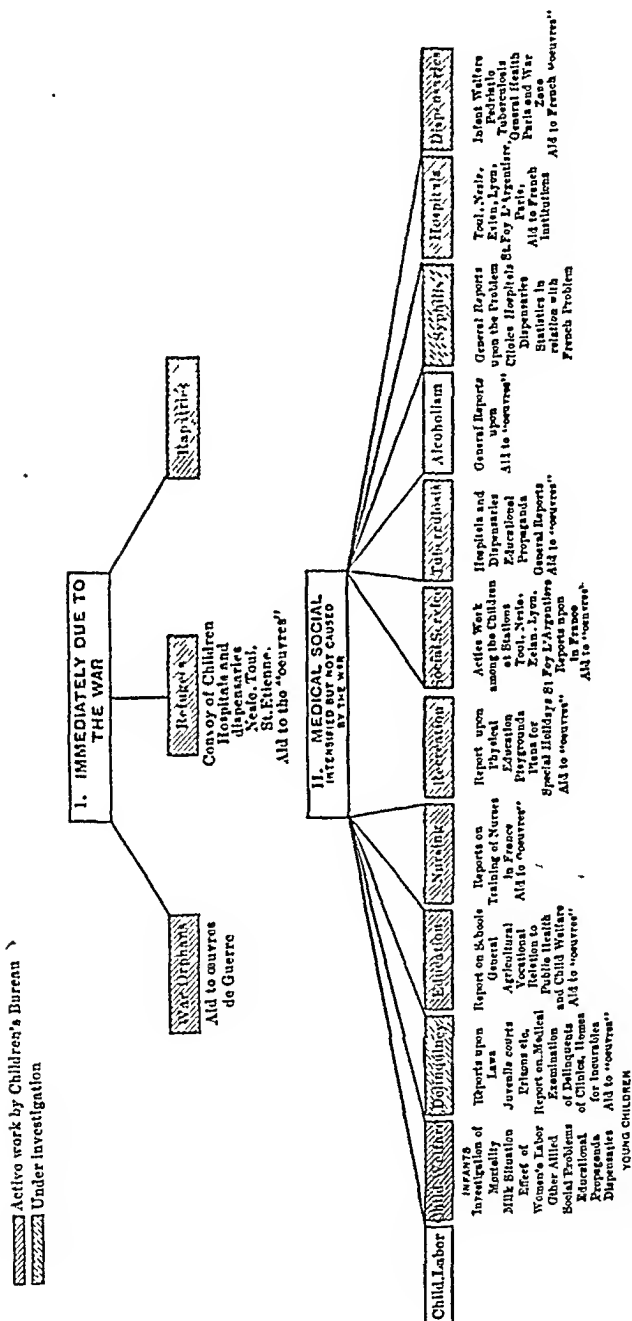


CHART IV.

pital, have been most eager for the help and coöperation of the Children's Bureau.

The plan now under way is to establish a clearing-house hospital and dispensary for children here in Paris. Hundreds of refugee children come from the north of France through Paris and a place of observation and of care for these children is greatly needed. This has been felt by all the different agencies, both French and American, dealing with the present acute problem of the refugee child. Again, the size of the problem seems almost overwhelming, but it is only by meeting one need at a time as thoroughly as possible that the service can be given. It is the hope of the Children's Bureau to have the Paris Clearing-house Hospital and Dispensary established and ready for work in another month.

I have already spoken of the assistance, medically, that the bureau is glad to give to French appeals for help. Besides the two dispensary services, one at Levallois-Perret and one at Grenelle, referred to in connection with Dr. Marfan and Dr. Guinon, the Children's Bureau has supplied a doctor for the Franco-American Committee for the Protection of the Children of the Frontier in the splendid work they are doing among about 1600 children. Two doctors of the Children's Bureau have been assigned to Italy for the immediate relief work there. One of our women doctors has been loaned to the work of the English and American Friends in a hospital for women and children which they are running in the War Zone.

#### V.—TUBERCULOSIS, EDUCATION, PUBLIC HEALTH.

Much the largest medical problem confronting France today is tuberculosis. In view of this, dispensaries for the care of the tuberculous are being organized by the Red Cross Bureau of Tuberculosis in conjunction with the Children's Bureau, which is starting work for infants and children in all the tuberculosis dispensaries to which I have already referred. The preventive side of this work for children is one of the most important tasks of the Children's Bureau. If we are to prevent the spread of tuberculosis we must teach the children and their parents such habits as will tend to prevent the dissemination of infection. This purpose can be accomplished by means of education in hygiene and public health, by developing community coöperation in health matters and building up the methods by which tuberculosis or any other infection can be checked in the home. For this purpose the Rockefeller Commission and the Children's Bureau are equipping a Bureau of Public Health Exhibits. These exhibits are modeled after the best types of American Child Welfare Work, most carefully and thoroughly adapted in form for presentation to the French mind. These exhibits include traveling exhibits on large motor trucks, carrying models, photographs, moving pictures and literature. The first week in December this exhibit makes its first trip, the way

being carefully prepared by an advance agent. This educational service of the Children's Bureau is in the hands of Mr. Philip S. Platt, and I feel that it is very close, in its importance to the French, to the immediate medical care. The work has been most carefully done. The Ministries of Munitions, of Education, of Labor and of the Interior are all in most hearty sympathy and coöperation. The League against Infant Mortality, the Lannelongue Institute of Social Hygiene, the National Labor Syndicate, the National Tuberculosis Committee, the Department of Health, the Museum of Hygiene and many private individuals, doctors and lay people have been consulted and all the material both of lectures, books, posters and leaflets has been made as thoroughly French as possible.

Already the attempt to fight tuberculosis by these means has been started in one of the smaller cities of France, at Bourgen Bresse, where, in October, an exhibit has been carried on with lectures and moving pictures and the other well-known features of a public health exhibit focussed especially on the problems of tuberculosis and child welfare. It is most encouraging to see this type of work developing in France, and we are sure of some lasting effect from such an educational campaign, because the French doctors and workers know its value and only need our help in getting such education to the people.

French workers prominent in the field of public health believe that one of the greatest needs of the time is for public health visiting nurses. Accordingly the Rockefeller Commission and the Children's Bureau, the Tuberculosis Bureau and the Bureau of Refugees, with Dr. Richard Cabot as Medical Head, are aiding in the development of visiting nursing in connection with the French training schools for nurses. Courses in visiting nursing and social service work will be given in connection with all the dispensaries, with special reference to tuberculosis and infant welfare. Lectures will be given; home visiting and follow-up work will be organized, together with an opportunity for experience in some of the French hospitals now maintained almost entirely by American nurses and American doctors. In this work the Children's Bureau is fortunate in having the assistance of Miss Elizabeth Ashie, whose sane and broad leadership in matters of public health and social service has distinguished her for twenty years in San Francisco, and Miss Harriet Leete, who has helped to develop in Cleveland what is probably the best of all nursing centers for child welfare. We hope to make a demonstration of permanent value. Indeed, of all the lines of work in which the Children's Bureau is engaged its public health nursing and the Model Health Center in which we shall have a large share, will be the most permanent and lasting.

Under Miss Maude Cleveland, of the faculty of the University of California, a splendid program of recreation for all our different

children's centers has been worked out, and Miss Cleveland is devoting all her trained skill to the problem of play for these tired and frightened French children. In our hospitals and convalescent homes, trained recreational workers are lightening the problems by adding to the normal happiness of each child in helping them to play.

Another large section of the Children's Bureau is given to the question of aid to other societies doing medical and welfare work for children. We are here to help the French in the way they want to be helped so far as it is possible, and the bureau has had over 200 applications for help from different societies and institutions for the care of children who are suffering from war conditions. In this section the bureau has the assistance of Mrs. William H. Hill, Secretary of the Franco-American Committee for the Protection of the Children of the Frontier. Mrs. Hill's long experience in France and sympathetic knowledge and understanding of the different works being carried on for children make her invaluable to the bureau in the difficult task of investigating and selecting the works we are able to assist.

The efforts of the Children's Bureau, then, are already numerous. The type of medical assistance that we need is general rather than special, except in its model health center, where only specialists will be needed. Elsewhere in its work with the "rapatriés" and in the Zone des Armées we need physicians and nurses with general training rather than specialists.

Perhaps the most lasting work which the Children's Bureau will accomplish will follow the work now in progress in its coöperation with the National League against Infant Mortality. The chief and the associate chief of the Children's Bureau, Dr. W. P. Lucas and Dr. J. H. Mason Knox, are attending weekly committee meetings of La Ligue contre La Mortalité Infantile, and coöperating in every way with plans under development for a national campaign against infant mortality. The child life of a country is the second line of defense. It must be preserved at any cost and strengthened in every way if we would keep any nation truly prepared to meet future demands. The conservation of child life is as much a part of this great conflict as the maintenance of armies. It is for the future freedom of the children of today and of tomorrow that our Allied Armies struggle at present. The struggle must not be in vain. From such ideals at home the Children's Bureau<sup>2</sup> of the American Red Cross sprang. Toward the consummation of such ideals the Children's Bureau will continue to work.

<sup>2</sup> The present (December 1, 1917) staff of the Children's Bureau numbers 37 doctors, 41 nurses, 14 aides, 12 social service, educational and recreational workers, and 12 clerical and business staff, total, 116.



**War Neuroses.**—MACCURDY (*Psychiatric Bulletin of the New York State Hospitals*, July, 1917) says although the term "shell-shock" has been adopted officially by the British War Office, as the diagnostic term to cover all neuroses arising among officers and soldiers of the armies, the name "war neuroses" is considered more advisable by the writer. In a little over 100 pages he gives a comprehensive survey of these conditions, with detailed reports of 27 cases. These were observed in British hospitals during a period of two months, and in their number were both officers and men. The two main types of war neuroses are conditions of anxiety on the one hand and of simple conversion hysteria on the other. The former may also be designated as anxiety states, for anxiety is the most prominent and consistent feature in the clinical picture. These cases bear most resemblance to what is frequently termed "neurasthenia" in civil practice. The first sign of an approaching neurosis is fatigue. This is not ordinary fatigue, which is completely removed by rest, even of quite brief duration. The conditions producing the fatigue are both physical and mental. Those on the physical side are the obvious ones of long hours of duty, combined often with irregularity of meals, shortness of water supply, exposure to extremes of temperature, and to frequent storms. Important as these are, however, they are probably of less influence in the production of neurotic fatigue than are the purely mental influences. The most common and important of these is the strain of continuing in a dull routine that demands a constant alertness, a speediness of decision, complete self-confidence, and a spontaneous eagerness; and this mental attitude must be maintained for hours at a time, even days, without sleep, often without the distraction of food, and in the face of constant danger. Other factors contributing to the development of fatigue are personal antagonism to an associate, susceptibility to particular discomforts, such as presence of vermin or bad odors, particularly of unburied bodies. It is a striking fact that anxiety conditions in a pure state occur almost exclusively among officers, and this may well be because of their greater responsibilities in the mental sphere. It is their task not merely to keep their own feelings in subjugation but to inspire the men beneath them with courage and enthusiasm. The various stages in the progress of the conditions are followed out in detail by the author, with illustrative cases. The role of concussion in the production of anxiety states has been emphasized by the more organically-minded neurologists. But in this series of cases, less than a fourth showed concussion as a preponderating factor. Two-thirds had no suggestion whatever of concussion in their history. Attempts should be made by neurologists to discriminate between the symptoms which are to be accounted for on a physical basis and those more purely psychological in origin. The treatment of the anxiety states is effective in a large number of cases, and some of the guiding points are here outlined. The conversion hysterics are much simpler in mechanism than the anxiety states, and it is less difficult to understand them and to treat them. Conversion neuroses may be defined as neuroses in which there is an alteration or dissociation of consciousness regarding some physical function. The term is used because an idea is transferred over into a physical symptom. The cases are confined almost entirely to privates and non-commissioned officers, and the more important symptoms

are those which obviously provide the patient with a relief from active service. Mutism is the commonest, possibly, and deafness is fairly frequent, and next in importance are motor disturbances. Fatigue is usually the first symptom discoverable, but it is not often so severe as in the anxiety cases and its effects are not so well marked. More frequently there is a history of pure diurnal dissatisfaction. There is almost always some weariness and a distinct antagonism to fighting. This attitude of antagonism with some idea of release constitutes the background of the hysteria. Various types of treatment are in common use. Any form of suggestion, particularly hypnotism, is often effective in the removal of the immediate symptoms. Drawbacks to this method and indications for other lines of treatment are discussed. Under the heading of heart neuroses are considered briefly that condition which has been termed "soldier's heart" or "disordered action of the heart." This is found in a rather large group of men who are invalided from the trenches with heart symptoms but who show no signs of valvular trouble. The cardinal symptoms are weakness, shortness of breath, palpitation, and dizziness. Some think the condition a form of war anxiety neurosis. The patients examined by the writer were not neurotics in the narrow sense of the word. These war neuroses are apparently a corollary of modern methods of fighting. There is something in the modern trench warfare, combined with the appalling artillery fire, which tends to produce a condition of what might loosely be termed neuropsychic instability. In the Boer war nothing similar was observed, and the first reports of these conditions came from the Russo-Japanese war.

W. H. F. A.

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**Infective Jaundice.**—DAWSON, HUME, BEDSON (*British Med. Jour.*, September 15, 1917) state epidemics of jaundice have been of frequent occurrence among armies in the field. Early in this war the authors began to observe severe cases of jaundice in which there were high fever, hemorrhages, enlargement of the liver, and a tendency to febrile relapses, which in no way conformed to the typhoid group. During the same period, Japanese investigators, Inada and Ido, and their co-workers had found by animal experimentation that cases of febrile icterus in Japan were caused by a specific organism which they named *Spirocheta ieterohemorrhagiae*. This is described in two recent papers in the *Journal of Experimental Medicine*, 1916. Following the line of investigation suggested by this discovery, the present authors have been able to prove that the infectious disease usually accompanied by jaundice which they had been studying among the French and British troops in France is also due to this spirochete. In a case of moderate severity the following features are noteworthy: Sudden onset, vomiting with high fever, marked prostration, occurrence of melena and hemoptysis, hemorrhagic herpes on the lips, appearance of jaundice on the fourth or fifth day which increases up to tenth or twelfth day, fall of temperature at the end of eleven days and the finding of typical spirochetes in the urine after ten to fourteen days. The urine usually contains a large quantity of bile, and albumin can nearly always be detected. The liver is usually considerably enlarged but the spleen is practically unchanged. The mortality is estimated at 4 to 5 per cent. Their treatment thus far has been purely symptomatic. The

jaundice appears to be due to obstruction, and not of hemolytic origin. The mode of excretion as studied in the guinea-pig by the Japanese workers is by the bile, feces and urine, but it is only in the latter that it can be demonstrated readily under the microscope. Infection may take place through the skin, or by the mouth, and the infective organism is probably spread mostly by the urine and feces. It has been noticed that the majority of cases come from localized portions of the front-line trenches, and that these trenches were always damp or wet, because it was impossible to drain them properly. When troops were moved out of these trenches, they ceased to have cases of jaundice, and when fresh units were brought in, although there were no cases among them before, the disease soon developed. In addition to the patients themselves distributing the organisms, it has been found by the Japanese investigators that 38 per cent. of the field rats coming from the areas to which jaundice was epidemic showed the presence of the spirochete. So that in the trenches the omnipresent rat may also act as a carrying agent and spread the disease by means of its urine directly or indirectly. Early diagnosis by finding the organism is not easily possible. Up to the seventh day it may be looked for directly in the blood with dark-ground illumination but it is difficult to locate owing to the small number of organisms present. The spirochete does not appear in the urine until about the ninth day and then only in very small numbers, but the number increases rapidly and reaches the maximum at about the thirteenth to fifteenth day of the disease. The most satisfactory diagnostic test is by injection of the patient's blood or urine into the guinea-pig. In a positive case after an incubation period of six to twelve days, the animal develops the disease and dies. On account of the time required by this test—the most decisive of all—the main reliance in diagnosis has to be placed on the correct interpretation of the clinical signs and symptoms. W. H. F. A.

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**Epidemiological Study of an Outbreak of Measles.**—**LIEUT.-COL. EDWARD L. MUNSON, M. C., U. S. A.** (*Military Surgeon*, xl, 666; xli, 63, 186, 257), gives the results of a study of an outbreak of 444 cases of measles among 13,773 troops. He calls attention to the sanitary importance of measles among troops. It is his belief that the disease should be classed among the respiratory diseases instead of among the eruptive fevers, and is of the opinion that an epidemic of respiratory diseases should be regarded as a warning of an outbreak of measles. The exciting cause is believed to be a vegetable organism on account of the variable period of incubation, irregularity being characteristic of the development of vegetable rather than of animal life, and because it is more or less alike in its requirements for perpetuation and development to the exciting causes of other respiratory diseases of bacterial nature. The duration of the infectivity of the disease is that of the catarrhal stage. This undoubtedly varies and the length with few exceptions seems almost impossible to determine. Many cases were preceded by "coughs" and "colds" of obscure origin and when one clinical condition merged into another often is not possible to say, indeed rapid rise in the respiratory sick rate should serve as a warning that an outbreak of measles is impending. It is believed that the

period of infectivity comes at least three days before the rash appears. The apparent incubation period was thirteen to fourteen days, the wide variation given in some text-books being never observed. Of the contributory causes, the environment in the tent is believed to have been the most important. Cold weather brought about the use of stoves and led to poor ventilation, with the result that the respiratory sick rates increased promptly and extensively. There is no direct effect of the weather on the cause of the disease, but it acts indirectly through the mode of life of the individual. Spitting was probably a fruitful way of transmitting measles. There is reason to believe that virulence, size of dose, and repetitions or duration of exposure have much to do with susceptibility or immunity. This is merely an hypothesis at present but clinical experience is in favor of it. M. J. R.

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**Effect of Marching on the Rates for Non-efficiency of Newly Raised Troops.**—LIEUT.-COL. EDWARD L. MUNSON, M. C., U. S. A. (*Military Surgeon*, xl, 171), states that the amount of disability in a marching command is an expression of the care with which the troops were selected, the efficiency of their training and the thoroughness with which unfits were eliminated prior to the beginning of a march. When these factors did not obtain in like degree in different organizations the results were diverse and important, as shown by curves of graphic charts of admissions to sick report. Foot troops require particularly careful examination before being allowed to participate in campaign, especially as to their fitness as burden carriers; this includes freedom from disease, muscular development, condition of feet and general physical stamina. In the mounted service much of this does not apply. The mounted man is himself the burden and not a burden carrier. Weak feet, poor physique or slight ailment do not necessarily disqualify for ordinary campaign conditions. Physical standards are allowed to fall too low in many cases. Sufficient time should be taken to properly examine the men and exclude all unfits. After enlistment all substandards should be specifically looked for at the first opportunity and eliminated if there is reason to believe they will fail to accomplish the requirements of military service. Greater care is required in making inspections for concealed disease. There should be more training in marching. It will shake out men whose unfitness would otherwise be concealed. The idea that the disease is not transmitted through fomites is opposed. It is believed that immediate infection is possible under living conditions in military organizations and that every chance for such should be removed. Military life also affords many favorable opportunities for direct infection. Overwork and lowered resistance probably have little effect on susceptibility except through their interference with discipline. Troops from the country and small towns have a greater susceptibility to the disease. The exhaustion of non-immunity or not enables prophesies to be made as to whether or when more cases will occur. It is believed that improvement in general sanitation and ventilation prevented many cases, as shown by the incidence of the disease; 54 per cent. of the susceptibles in one group where discipline was lax and general sanitation poor had measles, while only 6 per cent.

in another group where there was better discipline were attacked. Discipline is the mainspring of sanitation. The quarantining of suspects prevents epidemics. Few prove negative and the time saved is valuable. The human factor in quarantine makes it inefficient unless there are physical obstacles to communication. A measles census to ascertain the number of susceptibles is desirable and it should be taken promptly on account of the tendency toward evasion where quarantine is being established. It is believed that no disinfection is necessary other than sunlight and ventilation. Early diagnosis is valuable. Attention is called to the danger of measles in causing a particularly fatal type of pneumonia.

M. J. R.

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**The Nutritive Value of Margarines and Butter Substitutes.**—HALLIBURTON and DRUMMOND (*Jour. Physiol.*, 1917, li, 235) recall that in 1915 Osborne and Mendel found that oleomargarine, as prepared from beef fat, contained the alcohol soluble accessory growth substance found in butter fat. The authors have given to rats a diet of casein, starch, salts, agar, yeast, and oleomargarine, and they found that this diet promotes normal growth and reproduction of species, and concludes that this fat is the nutritive equivalent of butter. Vegetable oils, however, have not the same nutritive value. When in the above diet a substitution of oleomargarine is made by any one of the following: coconut oil, cotton-seed oil, arachis oil, hydrogenated vegetable oils, by nut butters prepared from crushed nuts and vegetable oils—there is no proper growth of young rats. In other words, these materials contain little or none of the fat-soluble accessory substance. The authors summarize the practical results of their work as follows: "But when we approach the subject of the dietary of the poorer classes the question is a more serious one. In ordinary times the consumption of beef dripping, which is considerable among the poor, would to a large extent supply the lacking properties of a vegetable-oil margarine. But at the present time beef itself is expensive and the opportunities of obtaining dripping are therefore minimized. At the same time the three important foods for children already enumerated (milk, butter, eggs) have risen in cost, so as to be almost prohibitive to those with slender incomes. The vegetable-oil margarines still remain comparatively cheap, and the danger is that unless measures are taken to ensure a proper milk supply for infants at a reasonable charge, these infants may run the risk of being fed, so far as fat is concerned, entirely upon an inferior brand of margarine, destitute of the growth-promoting accessory substance. It would be truer economy even for the poor to purchase smaller quantities of an oleo-oil margarine if they cannot afford the luxury of real butter."

G. L.

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**Section of Surgery of the Head, Surgeon-General's Office.**—A summary of the work accomplished by the Section of Surgery of the Head in the Surgeon-General's Office can be considered appropriately under the following heads: *Organization, Personnel, Activities, Results.* The Council of National Defense authorized the Subcommittee on Ophthalmology, April 26, 1917. The personnel of this committee was as follows: Dr. James Bordley, Jr., chairman; Dr. George E.

de Schweinitz, Dr. Nelson M. Black, Dr. Walter R. Parker, Dr. Allen Greenwood, Dr. William H. Wilmer.

A committee of Otolaryngologists had been formed by the national societies to secure the services of competent ear, nose and throat specialists. The personnel of this committee was as follows: Dr. Charles W. Richardson, Chairman; Dr. Harris P. Mosher, Dr. Burt R. Shurly, Major Theodore C. Lyster, U. S. A.; Surgeon G. E. Tribble, U. S. N. August 15 this committee was authorized by the Council of National Defense as the Subcommittee on Otolaryngology.

With the idea in view that the injuries of the head seldom involve one structure it was deemed wise for these two committees to join forces for the purpose of devising the best means of concentrating all the activities devoted to surgery of the head. To develop further the work, July 7 the executive committee of the Council of National Defense added to the Subcommittee on Otolaryngology an oral surgeon, and to the Subcommittee on Ophthalmology a brain surgeon, these committees acting as a joint body to include all cases that could be classified under the division of surgery of the head.

The Surgeon-General had already contemplated such a plan and had assigned Major T. C. Lyster to the duty of making a thorough study of it. After a careful investigation Major Lyster requested the assignment of members of the joint committee for duty in the Surgeon-General's Office to assist in this work. Major Nelson M. Black was put in charge of ophthalmology, Major Harris P. Mosher in charge of otolaryngology, Major Vilray P. Blair in charge of oral and plastic surgery, Captain Charles Bagley, Jr., in charge of brain surgery.

The first activity engaged in by the committee was the listing of all the known specialists throughout the United States represented by the various subsections of the Section on Surgery of the Head and by preparing an indexed catalogue of these specialists. In determining the availability of applicants for service, assistance was rendered by an advisory committee which consists of well-known specialists in different parts of the country, to whom letters were sent requesting specific information. Through this means many of the most conspicuous men in the profession have joined the Medical Reserve Corps and have been assigned to duty in charge of the various Subsections on Surgery of the Head in the cantonments. Under them will be placed men of less experience who will be trained and later assigned to service in the base hospitals abroad.

Another duty of this sections is to suggest plans for a special head hospital pavilion to be erected in each national cantonment and to standardize the instruments and equipment to be used therein.

In addition to the cantonment hospital a special head hospital of one thousand beds was authorized by the Surgeon-General to be constructed and operated in France. This hospital is to include not only facilities and equipment for the care of the head surgical cases, in the way of operating room, laboratories, roentgen-ray department, etc., but it will have a complete optical shop for the grinding and repair of lenses for use in spectacles and various instruments as well as a complete instrument shop for the care and repair of the instruments of the entire plant. In order to simplify storage, transportation, etc., all instruments and apparatus have been standardized as much as possible. The lenses

to be worn by the soldiers, for instance, are all to be of the same size and shape. The frames will be carried in three stock sizes, which will permit of proper adjustment to any case. Plans for the organization of the army hospital have been studied and suggestions made, when requested, as to the personnel necessary for the work of the head section. The Subsection on Oral and Plastic Surgery suggested the plans for dental operating rooms, which are to be included in the special hospital building.

The visual and hearing requirements of the various branches of the Army, together with methods of detecting malingerers, have been submitted for study and suggestions. Arrangements are to be made to provide for the work of dental oral surgeons by the Section on Surgery of the Head.

The following-named publications have been authorized by the Surgeon-General:

The Subsection on Brain Surgery prepared a book on *War Surgery of the Nervous System*, which was published by the Surgeon-General's Office and printed at the Government Printing Office.

The Subsection on Oral and Plastic Surgery revised Blair's book on *Surgery and Diseases of the Mouth and Jaws*.

The Subsection on Ophthalmology edited a *Manual of Ophthalmology*. Three members of the section also furnished the manuscript to the Committee on Publication of the Council of National Defense of a book entitled *Ophthalmic Military Surgery*, with chapters on trachoma and tests for the detection of malingerers.

The Subsection on Otolaryngology has in preparation a *Manual of War Surgery in Otolaryngology*.

On request there was furnished an outline of the course of lectures to be given the officers in the cantonment base hospitals by the senior officer in each section, together with a list of books for a reference library.

In two of the subsections, namely, that on brain surgery and oral and plastic surgery, there were not enough available surgeons sufficiently trained in these specialties to qualify for the responsible positions they were to fill. To meet this demand, schools were established and intensive courses of study instituted at the following-named places: Officers' School of Plastic and Oral Surgery, Northwestern University Dental School, Chicago, Ill.; Thomas W. Evans Museum and Oral Dental School of Surgery, University of Pennsylvania, Philadelphia, Pa.; Neurosurgical School, Chicago, Philadelphia, New York; Neurosurgical, Plastic and Oral Surgery School, St. Louis, Mo.

Regular courses are being given in these schools by men conspicuous in the profession for their teaching experience. The courses are open (1) to those of large surgical experience, the object being to add special technic to their knowledge; (2) to develop the work in younger men who will be placed as assistants.

Officers of the Subsection on Brain and Plastic and Oral Surgery are being assigned to the cantonment hospitals of this country and to each base and evacuation hospital going overseas.

For the purpose of elucidating some of the problems of neurosurgery, especially infections of the brain cord and coverings, a laboratory was established September 1 at Johns Hopkins Medical School, Baltimore,

Maryland. The members of this laboratory staff are now diligently working on investigations of procedure and methods of treatment that can be adopted for general use in war surgery:

As a result of the activities of the Section on Surgery of the Head, 568 officers have been assigned active duty in the National Army and the National Guard Cantonment Base Hospitals or are being given special training for service at home or abroad.

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**Effects of Submarine Duty on Personnel.**—Assistant Surgeon WALTER W. CRESS, U. S. N. (*Military Surgeon*, xl, 699), considers the hygiene of the submarine an interesting field and observes the lack of available literature on the subject. He conducted observations on the ventilation of the submarine and on the effect of submarine duty on blood-pressure, weight and hearing of the crew. Bacteriological examinations of the air, under different conditions under which the submarine acts, showed the presence of far fewer bacteria than in that of dwellings and battleships, and the number of microorganisms was greatly reduced when the ventilation was at its poorest as compared with the number present when it was at its best. It is believed that this low content is due to the high humidity and the absence of dust particles and the aspirating action of the engines. Discomfort experienced while submerged greatly exceeds that experienced when running on the surface. This is due to the rise in humidity and temperature as a result of the rapid evaporation of the battery fluid and the higher speed of the dynamos. The fumes of unburned oil from the exhaust when charging the batteries is considered likely to give rise to a transitory albuminuria. While the number of blood-pressure readings was considered too small for the drawing of definite conclusions, it is believed that long, continuous duty on submarines is conducive to high blood-pressure. The cause is not determined, but may be due to strain, lack of exercise and overeating, excessive use of tobacco or coffee or fatigue. A small loss of weight was noted after long trips, but this is not attributed to submarine duty *per se*, as such usually occurs during the first few days at sea on any vessel. An occupational deafness occurs in many individuals on submarine duty as a result of the vibratory movements and noises and the conditions favorable for the production of epipharyngeal and middle-ear catarrh. It is advised that thorough examinations be made of men before they are assigned to submarine duty and that no man be accepted who has had syphilis or the sequelæ or complications of gonorrhea. M. J. R.

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**Smoke and Powder Gases in Naval Warfare.**—Surgeon D. N. CARPENTER, U. S. N. (*Military Surgeon*, xxxix, 461), concludes that there is danger to the personnel in naval action from powder gases in the enemy's explosive shells. This danger is greater in closed gun compartments than in turrets, and the gases may be distributed to all parts of the ship through the ventilating system. Owing to the positive internal pressure of the turrets there is no contamination of the turret air from the ship's own gun-fire. Owing to the possibility of fires being started from shell impact and explosion there is danger from smoke gases. Perforated funnels, ventilators, etc., may cause smoke contamination of any part of the ship, with serious effect



on the personnel. The fire-room force is also exposed to possible contamination from the furnace fires and coal bunkers. To prepare for such danger it is advisable to provide a liberal supply of a simple type of respirator to be used in the gun compartments, handling rooms, fire and engine rooms, turrets, etc. Suitable helmets should be provided for the use of the repair party in fighting fires; additional electric fans and blowers should be placed in closed gun compartments to be used in emergency, and oxygen cylinders should be provided for the use of the medical department in cases of asphyxia. M. J. R.

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**The Lobar Pneumonia Problem in the Army.**—Major HENRY J. NICHOLS, M. C., U. S. A. (*Military Surgeon*, xli, 149), considers lobar pneumonia an especially important disease among soldiers, and states that it is to be expected in large camps in the winter months. He reports an epidemic and states that some suggestions of progress were reached which should improve the method of handling pneumonia in the Army. Through the differentiation of types or strains of the pneumococcus it has been shown that the majority of cases of lobar pneumonia are due to the introduction from without of epidemic types of the organism. This has thrown light on baffling questions of epidemiology; it is now possible to trace the spread of infection by types and to detect infected contacts and "carriers." The question of preventive inoculation can be approached with some confidence in the reliability of type immune reactions. Inclusive evidence as to the value of specific serum heretofore has been due to the lack of knowledge concerning types. The use of type serum for a type infection has greatly reduced the mortality. Direct evidence of contagion has been demonstrated, based on the determination of types. Pneumonia is now classed with meningitis and diphtheria, with the same method of transmission and problem of prevention. If effective the use of vaccination for prevention is considered a far more promising measure than isolation. M. J. R.

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**Reorganization of the Civilian Hospital on a War Basis.**—SMITH (*Modern Hospital*, October, 1917) states that although present plans do not contemplate the use of civil hospitals to any great extent by the Medical Department of the Army, except in the event of a great emergency, certain suggestions may be made to civil hospitals preparing to be of service during the war. They should offer to the Government as many beds as possible, but they should be actual beds, readily available, and in sufficient number to be worth consideration. The size of the staff should be cut to the minimum in order to release as many physicians as possible for military service. The intern service should be organized on a one-year basis, in order to comply with the official regulations. They should prepare for the release of as many nurses as possible. They should admit as large classes of nurses as possible and prepare, if the emergency should arise, to graduate at least a part of the senior class of nurses early. They should be prepared to train nurses' aids whenever called upon to do so.

W. H. F. A.

## REVIEWS

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A HANDBOOK OF PRACTICAL TREATMENT. Edited by JOHN H. MUSSER, JR., B.S., M.D., Associate in Medicine in the University of Pennsylvania, and THOMAS C. KELLY, A.M., M.D., Instructor in Medicine in the University of Pennsylvania. Volume IV. Pp. 1000. Philadelphia and London: W. B. Saunders Company, 1917.

IN this IVth volume is brought up to date, under the same editorial names, the valuable work of the late and lamented editors of the first three, which were published in 1911. In so far as possible the contributors to the original volumes have in this one either indicated such new features of treatment as have been presented up to this time in the literature or have entirely rewritten their sections; and in those instances where death or other cause has prevented former authors from doing this, others have taken their places. Furthermore, distinctly new matter has been presented by special workers in their individual fields of study.

The introductory chapter upon the modern treatment of disease is contributed by Dr. Alfred Stengel, who reviews broadly the development of our present conception of medical treatment, and discusses briefly certain of the newer methods. Fortunately the sections by Dr. J. William White and Sir Lauder Brunton were revised for this work before their deaths, and appear under their names. Dr. Leonard G. Rowntree, as a new contributor, has completely revised the article upon nephritis, devoting 110 pages to this subject and presenting four very helpful charts in explanation of some of the newer methods of investigation and treatment of this disease. The Surgeon-General of our Army contributes an exhaustive but concise chapter upon one of the subjects with which his name is closely identified, yellow fever. The subject of tropical diseases is entirely revised by Dr. Bailey K. Ashford, as is that upon electrotherapy by Dr. Charles S. Potts, and upon the surgery of the liver and gall-bladder by Dr. John B. Deaver. Dr. Joseph L. Miller has rewritten the chapter upon the diseases of the blood, and Dr. George Morris Piersol has made several contributions, revising certain sections of which he was formerly only a co-author.

Among the entirely new matter contained in this volume are

the treatment of cerebrospinal syphilis by Swift, hay fever by Goodall, acidosis in children by Howland and Marriott, occupational diseases by Thompson, governmental prophylaxis by Dixon, peridental suppuration by Smith and Barrett, and splenectomy in the anemias by Krumbhaar and Pearce. The reviewer is unable to think of any valuable medical or surgical practice that is not now discussed in these four volumes, and feels that the names of the contributors are significantly indicative of the illuminating manner in which the subjects are presented.

Not the least important feature of the work is the exhaustive index of 67 double-columned pages which it contains. It is fitting also to call attention to the complete and separate 218-page desk index to the four volumes which accompanies this one. Mechanically both the volume and the desk index are well done, the binding being good, the type clear, the tables well presented, and most of the illustrations excellent.

T. G. M.

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REST, SUGGESTION AND OTHER THERAPEUTIC MEASURES IN NERVOUS AND MENTAL DISEASES. By FRANCIS X. DERCUM, M.D. Second edition. Pp. 395. Philadelphia: P. Blakiston's Son & Co., 1917.

THIS volume is a revision of Volume I of the *System of Physiological Therapeutics*, edited by Dr. J. Solis Cohen. As its title indicates it concerns itself with the method of treatment of nervous and mental conditions.

To begin with, probably no one in this country has had a larger experience in the treatment of the neuroses than Dr. Dercum. To gain such results it is apparent that his methods must be successful, and therefore whatever he writes upon this subject should be of the utmost interest.

The book is divided into three parts: (1) on rest; (2) on therapeutics of mental diseases; (3) on suggestion. Each is divided into appropriate chapters. In the first part, which concerns itself with the subject of rest, the author discusses the chemical, morphological and physical changes which occur in the sick person. He then takes up the symptoms of the fatigue neuroses, then the special rest treatment as applied to the neurasthenic, giving in detail the methods to be employed. This chapter is particularly interesting because it gives in large part Dr. Dercum's experiences of many years. The nature of hysteria is then discussed. The author distinguishes between simple neurasthenia and psychasthenia and hysteria from hypochondriacal conditions. He inclines to Babinski's view-point as to the presence of symptoms due to the examination of the physician. These views, as many others, are being radically changed as the result of experience gained from the present war.

He then discusses symptoms and treatment of hypochondriacal conditions and the rest treatment of such conditions as chorea, epilepsy, paralysis agitans and organic conditions of the nervous system.

In the second part the prevention of insanity and the general principles of the treatment of the insane are first discussed and then treatment of the special forms of mental diseases. In the last division on suggestion the author takes up the ordinary forms of suggestion, then discusses all the special cults, including those of Mrs. Eddy. Lastly he discusses the psychoanalytical method.

This is an excellent book, full of common-sense methods for the treatment of all forms of nervous conditions, a copy of which should be in the hands of every physician. T. H. W.

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THE MASTERY OF NERVOUSNESS. By ROBERT S. CARROLL, M.D.  
Pp. 360. New York: Macmillan Company, 1917.

As its title indicates this volume concerns itself with the exposition of the nature of nervousness and its cure. The book has been written for the laity. The healthy, vigorous normal individual need not read it. It is only the neurotic, who seeks to master his nervousness, who will read such a work as this, because he thinks that from its perusal he can gain what he seeks—health. For such a person this work is valueless. It is not because this volume is not well written, for it is. The author apparently has had a wide experience and writes fluently and well, but practical experience has shown that for the neurotic all works of this character are of the greatest harm, for it is well known that such a person will apply every symptom to himself, for he is incapable of normal reasoning. For the physician it is not scientific enough. Many books of this kind have been published in the last few years. This is one of the best of its kind, but it is a pity that the author, who knows what he is talking about, should not have directed his energy in a more productive line.

T. H. W.

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SUGGESTIVE THERAPEUTICS. By HENRY S. MUNRO. Fourth edition, revised and enlarged. Pp. 481. St. Louis: C. V. Mosby Company, 1917.

THIS is the fourth edition of this work, the first having been reviewed in this JOURNAL some years ago. If repeated editions are an indication of the need of a book and of its success, then from these standards this book is a success, and there is need for it. Yet this book is altogether unscientific. It is written for the general practitioner. The text is in the conversational style, the author giving many examples of methods employed by him. Every phase of suggestion is discussed as applied to every sort of condition: for

example, hypnotism as applied to bronchitis, asthma, pneumonia, dressing of a painful wound; various operations, such as suprapubic cystotomy, dental surgery, insomnia, psychic impotency, the nausea and vomiting of pregnancy, alcoholism, pulmonary tuberculosis, etc. The methods used in applying hypnotism are given at length. Chapters are written on suggestion as an adjunct in the administration of anesthetics, on psychotherapy in relation to the expectant mother, the psychological factor, obstetrics and the technic of application. In the discussion of the sex phase the author goes into the subject at length. His advice is very good and method of the treatment of this phase is sound. The author differs from Freud not only in his principles but in the application of them, stating that the principles of Freud are limited and that the method advocated by him are harmful, etc. The author does not hesitate to state that his views are much better than those of Freud and that his experience is even larger. His knowledge of Freudian psychology is based upon his reading of certain articles, which he frankly quotes.

T. H. W.

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THE GROWTH OF MEDICINE FROM THE EARLIEST TIMES TO ABOUT 1800. By ALBERT H. BUCK, B.A., M.D., formerly Clinical Professor of Diseases of the Ear, Columbia University, New York; Consulting Aural Surgeon, New York Eye and Ear Infirmary. Pp. 582. New Haven: Yale University Press, 1917.

To attempt to present in one volume the history of the growth of medicine from the earliest times to about 1800 is a difficult task, but a most desirable one. Dr. Buck has been admirably successful, the work, although of less than 600 pages, including many illustrations, yet presents in plenty of detail all of the most important steps in the long story of medical history. Because of its brevity there is a continuity of thought and chronological progress which is so often lost in the maze of detail of more lengthy works. For this reason the book should become more and more popular with practitioners and undergraduate students of medicine who desire to reap ideals and stimulation from the lives and achievements of the masters of medicine.

The work is entertaining from beginning to end, is well illustrated and very clearly printed.

It is the first work published by the Yale University Press on the Williams Memorial Publication Fund, which was founded to enable "the Yale University Press to accept for publication medical treatises which deal with the historical and scientific questions of this branch of knowledge, but which, for sound business reasons, cannot be published on a merely commercial basis."

The reviewer begs to prophesy that in this instance the book will not only prove to be a credit to the author but a success on a merely commercial basis.

O. H. P. P.

# PROGRESS OF MEDICAL SCIENCE

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## SURGERY

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UNDER THE CHARGE OF

T. TURNER THOMAS, M.D.,

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UNIVERSITY OF PENNSYLVANIA; SURGEON TO THE PHILADELPHIA GENERAL  
HOSPITAL AND ASSISTANT SURGEON TO THE UNIVERSITY HOSPITAL.

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**Dakin's "Dichloramine-T" in the Treatment of the Wounds of War.**—  
SWEET (*British Med Jour.*, August 25, 1917, p. 249) says that he has  
treated some 80 cases with "dichloramine-T" (toluene-para-sulpho-  
dichloramine); some have been old cases with foreign bodies lying in  
the bone, and suppuration did not stop until the foreign body was  
removed. Fresh cases, in which enough integument was left to permit  
it, have been treated with dichloramine once and immediately closed,  
and have healed by secondary intention; 16 cases, old and fresh, were  
cultured after treatment with "dichloramine-T" for varying periods,  
of which 11 gave no growth whatever; of the 5 in which a growth  
appeared, 4 were old cases of deep bone involvement; the only growth  
was the *Staphylococcus aureus* in 4 cases and in 1 case the *pyocyanus*.  
The wound fills rapidly with granulation tissue of healthy color, which  
exhibits no tendency to become water-soaked and indolent; the skin  
edges grow in rapidly. The surgeons of the unit, with Dr. Sweet, are  
agreed that the wounds treated by "dichloramine-T" are in every way  
as satisfactory as they have seen under any method: The new "dichlor-  
amine-T" solution is made by dissolving the crystals of "dichloramine-  
T" in chlorinated eucalyptol and then diluting this solution by the  
addition of chlorinated paraffin oil. It is best applied by an oil spray,  
an ordinary hard-rubber or all-glass atomizer being the most practical  
method. It is of great advantage in wound treatment, even if the  
final results are no better, because it saves the pain of wound dressing;  
it affects an appreciable saving of dressing material; the amount of  
solution is of small bulk; the number of wounds which a surgeon can  
dress in a given time is far greater than by any other method; the  
elimination of the Carrel tube simplifies the dressing and the problem  
of the transportation of the wounded. The elimination of the Carrel  
tube saves the time of the nurse for the periodic flushing.

**Gunshot Wounds of the Knee-joint Treated in a Base Hospital.**—**CAMPBELL and WOLFENDEN** (*Lancet*, August 11, 1917, p. 185) say that these wounds have furnished one of the most difficult surgical problems of the war and their treatment, after nearly two and a half years, appears to be far from satisfactory. According to the anatomy and physiology of the joint the lines along which all treatment in septic cases must be directed are: (1) The lowering of intra-articular tension by evacuation of the exudate, thereby preventing the tracking of infection along the fascial planes; (2) the rapid overcoming of infection and the removal of infective material as soon as it is formed, thereby diminishing suppuration; (3) the promotion of the formation of adhesions, thereby limiting the area of infection and diminishing the surface for toxic absorption; (4) the removal of pressure from the articular cartilage, thereby diminishing the chances of its becoming eroded. Their present methods of treatment in severe cases are based upon three fundamentals: (1) Absolute rest and fixation; (2) the strictest asepsis; (3) the use of Carrel's method of wound treatment. With this method efficiently carried out they find that infection is most effectually counteracted; that organisms and the pabulum suitable for their growth are washed outward, even from the deepest parts of the wound; that ingress of sepsis from without is prevented, a most important consideration in the treatment of knee-joint cases; that pus forms only in small quantity; that adhesions of the synovial membrane form with great readiness; that the patient need only be dressed in twenty-four or forty-eight hours. Earlier their cases were treated by the saline method. Comparing the last series of results so gained with those obtained recently when using Carrel's method they find that in the latter the mortality is reduced to one-fourth and the number requiring amputation to one-eighth, although the cases treated by Carrel's method were, if anything, more severe. From their limited experience they are not disposed to advise excision of the joint as a method of treatment in septic arthritis.

**Surgical Methods of Dealing with Pelvic Infections.**—**CULLEN** (*Surg., Gynec. and Obst.*, 1917, xxv, 134) says that when an appendix abscess is opened the appendix can practically always be removed at the same time, provided the abscess is well walled off with gauze before an attempt is made to open it. In removing a large pus tube that is firmly adherent to the pelvic floor, it is better to begin by excising a wedge of the uterine cornu, and gradually freeing the mesosalpinx. The tube can then be lifted up as a straight rod and carefully walled off on all sides before it is shelled off from the pelvic floor. Soiling is reduced to a minimum. Pelvic drains that emerge from the vagina should be so arranged that they do not come into contact with the small intestine. Vaginal drains laid in the pelvis during an abdominal operation should not be removed, as a rule, before the fourth or fifth day on account of the danger of pulling down an adherent loop of small bowel. The vaginal drainage of a pelvic abscess may relieve the patient only temporarily. The development of other incipient abscesses may require several more vaginal operations before the inflammation subsides, and even then a subsequent abdominal operation may be necessary. No case of pelvic abscess should be irrigated. There is danger of rupture of

the abscess wall and of the escape of infectious fluid into the abdomen which will set up a general peritonitis. Postpuerperal infections are found, as a rule, in one or both broad ligaments. Those in the broad ligaments can be most satisfactorily opened extraperitoneally through a gridiron incision just above Poupart's ligament. Such accumulations should rarely, if ever, be opened through the vaginal vault.

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## THERAPEUTICS

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UNDER THE CHARGE OF

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**Clinical Studies on the Respiration. IV. The Vital Capacity of the Lungs and its Relation to Dyspnea.**—This paper by PEABODY and WENTWORTH (*Arch. Int. Med.*, 1917, xx, 443) is really a continuation of the preceding in which they showed that patients with heart disease became dyspneic more easily than did healthy subjects because of their inability to increase the depth of breathing in a normal manner. The inability to breathe deeply corresponds to a diminished vital capacity of the lungs as measured by the volume of the greatest possible expiration after the deepest inspiration. The investigators employed two different methods of measuring the vital capacity. One was by use of a calibrated recording spirometer, the other by the use of an ordinary portable spirometer. They determined that the position of the patient made no practical difference in his vital capacity. One hundred and forty healthy adults were studied. They were classified according to sex and height. Of the males there were three groups: Group 1 consisted of those persons 6 feet tall or over whose normal capacity was 5100 c.c. Group 2 consisted of men between 5 feet 8.5 inches and 6 feet tall with a normal vital capacity of 4800 c.c. Group 3 consisted of men whose height was between 5 feet 8.5 inches and 5 feet 3 inches, whose vital capacity was 4000 c.c. Though the vital capacity of some subjects was very much greater than that called for by their group position, only 1 of the 96 normal males had a vital capacity more than 10 per cent. below the appropriate normal standard. Peabody and Wentworth conclude that healthy males almost invariably have a vital capacity of 90 per cent. or more of the normal standard. The women were also divided into three groups: Group 1 measured over 5 feet 6 inches; vital capacity 3275 c.c. Group 2 measured from 5 feet 4 inches to 5 feet 6 inches, with an average vital capacity of 3050 c.c. Group 3 made up of persons who measured from 5 feet 1 inch to 5 feet 4 inches; vital capacity 2825 c.c. In five of these women the vital capacity was more than 10 per cent. below the appropriate normal, but in no case was it more than 15 per cent. below. 224 observations on 124 patients suffering from cardiac disease showed that the clinical condition of the patient, more especially the tendency to dyspnea varied directly with the degree to which the vital capacity was diminished.



Patients with a vital capacity of 90 per cent. or more of the appropriate normal standard adopted for their sex and height had little or no abnormal tendency to dyspnea. Patients with a vital capacity of from 70 to 90 per cent. of the normal became short of breath on unusual exertion and must lead a restricted life, although many of them can do light work. Patients with a vital capacity of from 40 to 70 per cent. of the normal become dyspneic on moderate or slight exertion, are rarely able to work, and frequently suffer from cardiac decompensation. Those with vital capacity of less than 40 per cent. are decompensated patients, usually confined to bed, and the mortality in this group is high. There is a close correspondence in the individual case between changes of vital capacity and variations in the tendency to dyspnea. In stages of decompensation the vital capacity falls, and with recovery the vital capacity rises. Comparatively slight changes in the patient's condition may manifest themselves in changes in vital capacity. Indeed it is possible by studying the variations in vital capacity to throw much light on the course and even on the prognosis of the disease. In various other diseases in which mechanical conditions interfere with the movement of the lungs, such as pleural effusion, cirrhosis of the liver with ascites, etc., the tendency to dyspnea corresponds closely to the decrease in vital capacity. This, however, is not true for the anemias, where the dyspnea appears to be due to the low hemoglobin content of the blood. In acute nephritis the vital capacity was not decreased below the normal. In chronic nephritis without evidence of heart disease and without history of dyspnea, vital capacity was usually within the normal limits. In cardiorenal cases where dyspnea was a prominent symptom, vital capacity was usually decreased in proportion to the intensity of the dyspnea. In diseases in which dyspnea is not a prominent symptom, such as acute and chronic arthritis, diabetes, hemiplegia, tabes, and in surgical convalescence the vital capacity is usually within the normal limits, although general weakness and old age may cause a slight decrease.

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**Clinical Studies on the Respiration. V. The Basal Metabolism and the Minute-volume of the Respiration of Patients with Cardiac Disease.**—PEABODY, WENTWORTH and BARKER (*Arch. Int. Med.*, 1917, xx, 468) report their observations on the gaseous metabolism and pulmonary ventilation of two groups of patients with heart disease. Group 1 consists of subjects in good or fairly good condition, in whom the vital capacity of the lungs was over 60 per cent. of the normal. Group 2 consists of much more severely affected patients in whom the vital capacity was 60 per cent. of the normal or less. The basal metabolism calculated from the oxygen consumption per square meter of body surface averaged 2.5 per cent. above normal in Group 1, and 12.8 per cent. above normal in Group 2. The average volume per respiration was less in Group 2 than in Group 1, and the average rate of respiration was higher in Group 2 than in Group 1. The minute-volume of air breathed averaged approximately 30 per cent. higher in the members of Group 2 than it did in those of Group 1. The relation is pointed out between the increase of the minute-volume of the more seriously affected patients and the decrease in the vital capacity of the lungs. Finally it is shown that this high minute-volume is a factor in the production of dyspnea in persons with severe heart disease.

## PEDIATRICS

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UNDER THE CHARGE OF

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**Hypertrophic Stenosis in Infants.**—HOLT (*British Jour. Children's Dis.*, xiv, Nos. 163-165) states that hypertrophic stenosis of the pylorus in infancy is a pathological entity and it should not be confused with other pathological conditions which may be accompanied by vomiting and occasional gastric peristalsis. Many of the milder forms recover under medical treatment. If improvement is not noticed in the course of two or three weeks of medical treatment, and those which show severe symptoms, surgical treatment is indicated. These symptoms demanding surgical attention are rapid loss of weight, persistent vomiting and forcible, gastric peristalsis and the presence of a palpable tumor and abnormal gastric retention. The value of the roentgen rays is not so great as the study of gastric retention. In cases in which the symptoms have persisted for several weeks before they come under observation are best treated surgically as soon as a diagnosis is made. The author recommends the simple external division of the circular muscular fibers as recommended by Rammstedt rather than gastro-enterostomy, divulsion, pyloroplasty and such operations. The Rammstedt operation has been shown to be of greater value than any other operation and even better than medical treatment. Growth and development are not interfered with by this operation. Cases not operated on usually show no symptoms after the first year, but are possibly the basis of pyloric obstruction later on in life.

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**Intradermal Reactions to Proteins of Infants Suffering from Gastro-intestinal Disease.**—GREER (*Arch. Pediat.*, xxxiv, No. 11) says that in children suffering from gastro-enteritis or atrophy 23 out of 26 gave definite intradermal reaction to lactalbumin of the cow. Three reacted positively to caseinogen. The much greater reactivity to lactalbumin is in agreement with the observation that almost all allergic milk reactions proceed better with lactalbumin than with caseinogen. These findings suggest that sensitization to cow's milk protein does occur in acute or chronic gastro-enteric disturbance and that such sensitization can be demonstrated by the intradermal injection of small amounts of these proteins, and, further, that the lactalbumin is the protein to which, probably, sensitization most easily occurs.

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**Meningococcus Meningitis in the Newborn with Interesting and Unusual Features.**—MILLER (*Arch. Pediat.*, xxxiv, No. 11). This case showed the following features: The onset, with conjunctivitis, which was mistakenly regarded as gonorrheal; the bulbous eruption in the second week of the disease; the prolonged latent period before

signs of meningitis were apparent (fourth week); the peculiar character of the spinal fluid (tapping is liable to be unsatisfactory in the newborn, as fluid does not flow readily from the subarachnoid space, and in this case gelatinized at once); the large number of punctures of the fontanel (10) in so young a patient, with no apparent ill effect beyond vomiting (the first two of these punctures were made into the ventricle and afterward, with the greater accumulation, the needle probably entered the subarachnoid space); the large amount of serum introduced (in all 260 c.c.), with no sign of serum disease; the remarkable sclerema-like condition of the skin, persisting throughout the attack; the apparent improvement in the clinical symptoms and the cerebrospinal fluid after the tenth injection of serum, with the subsequent return of active symptoms and death.

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## OBSTETRICS

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UNDER THE CHARGE OF

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**Labor Conducted under Gas and Oxygen in Two Cases of Lost Cardiac Compensation.**—GETTMAN (*Jour. Am. Med. Assn.*, February 17, 1917) reports the case of a multipara who for three years had suffered from heart disease, with difficult respiration and swelling in her limbs. For the seven months preceding, she had been unable to walk and could not sleep except in a sitting posture. On admission to the hospital, her hemoglobin was 58 per cent., the urine showed albumin and granular casts, and mitral insufficiency, with lost compensation, was present. The patient was pregnant eight and a half months. Her previous labors had been without difficulty and the pelvis was normal. For nine days she received medical treatment, and, when labor began, she was transferred to the obstetrical department of the hospital. The first stage of labor went fairly well, but, when expulsive efforts began, the patient became cyanosed and almost pulseless. Nitrous oxide oxygen were administered and the patient was delivered of a full-term, living child by version and extraction. She passed through this very successfully and improved for nine days when she suddenly developed cardiac dilatation and died six hours later. The second case was that of a primipara, aged forty-three years, who had mitral regurgitation for five years. She had attacks of cholecystitis at intervals, and eleven years before had ventral suspension for retroversion. There had been edema of the feet and legs for three months, and the patient slept in a sitting posture. On examination the heart was dilated and its action irregular and weak. The child was in transverse position, and, as the patient was a primipara, it was thought best to deliver by Cesarean section under gas and oxygen. This was done successfully, the patient enduring the anesthetic and the operation well. The child was at full-term and in good condition. Mother and child left the hospital in two

weeks. These cases demonstrate the fact that gas and oxygen were used successfully. Without wishing to deny the virtue of gas and oxygen, the reviewer must call attention to the fact that the same thing has been done successfully under other anesthetics. Provided oxygen be used freely, either chloroform or ether can be employed in heart cases for delivery. Anesthesia is an absolute necessity with these patients, and saves life during the strain of labor. The omission of an anesthetic would be followed by death during labor.

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**Labor Complicated by Occipitoposterior Positions Treated by Digital Rotation.**—PECK (*Am. Jour. Obst.*, March, 1917) contributes an article upon this subject, with illustrations, and believes that these cases can be best managed by digital rotation. He finds that the positive diagnosis of the exact position of the head is essential, and is best made at the beginning of the second stage of labor immediately after the rupture of the membranes and during the contraction of the uterus. Attempts at digital rotation before the vertex is engaged in the pelvis usually end in failure because conditions are unfavorable. Digital rotation should be applied during uterine contractions and after the occiput is upon the floor of the pelvis. Rotation should be gradual, and the effort may have to be continued through several uterine contractions before the occiput remains anterior. In some cases the occiput seems more movable when the uterus is relaxed, but then the fingers cannot exert their full power in rotation because the tendency is for the fingers to slip off the bony ledge from forward displacement of the uterus. After anterior rotation has been secured, no effort should be made to deliver the child for some time in order to secure molding of the head. Digital rotation may often be used preceding the application of forceps. By this means, a favorable position is obtained for the direct application of forceps to the sides of the head. Should attempts at digital rotation fail, no harm has been done to mother or child.

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**Drainage of Pus Conditions in the Pelvis during Pregnancy.**—REDER (*Am. Jour. Obst.*, December, 1916) believes that the most satisfactory evidence of the presence of pus in Douglas's cul-de-sac can be obtained by rectal examination. If there is a considerable accumulation, it is readily recognized, but if the quantity of pus is small, it may be necessary to examine with the finger without a glove. It is well to recognize these conditions as early as possible as the continued presence of pus in the pelvis during pregnancy is a dangerous factor. In choosing the method of operation, it is well, if possible, to drain the abscess through the rectum. The anus is first gently dilated and the rectum thoroughly washed out. The index finger without a glove finds the most fluctuating spot and a sharp-pointed bistoury is passed along the finger and cautiously introduced. As soon as the pus is encountered, the bistoury is withdrawn, and the point of a dressing forceps introduced into the opening. By spreading its branches, a hole sufficiently large to admit the end of a rubber drainage tube is readily made. This tube is retained for a week and then removed. The operation may be performed with, or without an anesthetic.

## GYNECOLOGY

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UNDER THE CHARGE OF

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**The Blood in Cancer under Roentgenotherapy.**—As a result of an extensive study of the blood of patients undergoing roentgen treatment for cancer, STEVENS (*Am. Jour. Roentgen.*, 1917, iv, 215) summarizes his preliminary report by stating that roentgen rays, applied in repeated large doses, with deep penetration, profoundly affect the erythrocytes of human beings, contrary to most of the reported experiments on small animals. This effect consists of a considerable diminution in number from the fourth to the sixth day after treatment, then with vacillations rapidly increasing in number until the tenth or eleventh day, so that there may be a decided erythrocytosis with some vacillations. This may be followed by another drop and in cases where several treatments have been given over several weeks, the figures may not fully recover their former level before the end of forty or fifty days. For the first few days after a treatment the lymphocytes are suppressed or destroyed by large doses of roentgen rays in the treatment of cancer. In favorable cases this is followed by a reaction with lymphocytosis between the third and seventh days which may continue almost uninterruptedly until the fourteenth day or it may stop short after the seventh day and reappear more strongly and persistently on or about the fourteenth day. There is a strong resemblance between the curves of these lymphocytic reactions and those which constitute the opsonic index. The treatment should probably not be repeated until the reaction is over, and the repetition of the dose should probably be governed by the reactions in the blood as well as in the skin, the former being much more sensitive than the latter. In some cases of cancer, the roentgen rays tend to stimulate a general (though probably temporary) immunity, if lymphocytosis is an indication of immunity. The action of the roentgen rays in cancer therefore would appear to be twofold—local, by destruction of disease cells, and general, by stimulating lymphocytosis and consequently resistance.

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**Surgical Hemostasis of the Female Pelvis.**—A most interesting stereoradiographic study of the vessels of the female pelvis was executed by FURNISS and MEYER (*New York State Jour. Med.*, 1917, xvii, 462), with three definite objects in view: (1) they desired to show the degree of anemia that could be produced by the ligation of certain vessels or certain groups of vessels; (2) to show the most effective methods of producing anemia for surgical operations, and finally to show the minimal amount of blood supply compatible with adequate tissue nutrition. This study was conducted by injecting into the arterial system a mixture of red lead and albolene, after the ligation of certain vessels. After the removal of certain ligatures, further injections were

made and other radiographs taken. This was continued until all the ligatures were removed. As a result of this work it was found that with ligation of the common iliac arteries, together with the ovarian arteries, the only vessel filled in the pelvis is the superior hemorrhoidal branch of the inferior mesenteric; release of the ligature on the external iliac makes little or no difference in the filling of the pelvic vessels. The internal iliac vessels can be filled through only one ovarian vessel. While branches of the last lumbar arteries and of the gluteal and iliolumbar branches of the internal iliac can be seen in close proximity, the passage of the injected mass from one to the other cannot be demonstrated. Had there been branches sufficiently large to pass the injected material, it should have been demonstrated by the injection when the common iliacs and the ovarians were tied. Therefore it would seem that a most extensive and dangerous ischemia would be produced by the ligation of the ovarians and common iliacs, or almost as complete an ischemia by the ligation of the ovarians and internal iliacs. The authors believe that bleeding would be lessened by the ligation of one ovarian and both internal iliacs, or both ovarians and one internal iliac, without seriously endangering the nutrition of the pelvis, provided that structures through which the vessels crossed the median line were not removed. Further, that possibly the ligation of the ovarian and both internal iliacs during a hysterectomy would leave an inadequate blood supply, and that ligation of the ovarian and the uterines would give good hemostasis and yet leave sufficient blood supply. Investigations of this nature should be greatly encouraged as the findings should be of considerable value to the gynecologist in dealing with cancerous growths in the pelvis, especially when using the newer cautery technics in which extensive ligation of pelvic bloodvessels is an important part of the procedure.

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**Preservation of Menstrual Function in Tubal Disease.**—Practitioners who have been watching the literature of recent years will remember that considerable attention has been paid to the subject of pelvic inflammatory disease in all its forms by Polak and his staff. In his latest contribution, POLAK (*Jour. Am. Med. Assn.*, 1917, lxi, 1938) states that while all are agreed that the retention of an infected uterus, after removal of infected tubes, is a menace to the woman's future health, he personally believes that when so much care is taken to preserve the function of ovulation, there should be like care in preserving the function of menstruation, as ovulation without menstruation contributes little to the patient's well-being. Sections through the uterus, between the fundus and internal os show practically no pathological changes in these inflammatory cases, but the greatest pathology in the uterus is to be found in the cervical glands and in the fundal region and pars interstitialis of the tube. In order, therefore, to clear the patient from these infective foci, many operators have been performing a panhysterectomy, which, to be sure, entirely rids the patient of the infection, but also deprives the patient of further menstrual flow. In order to obviate this unpleasant sequel, but at the same time to thoroughly rid the patient of her infection, Polak has been treating the cervix by linear cauterization or excision following which he attacks the tubes and fundus of the uterus by the method of Beuttner and Bell. This procedure consists of the ablation of both tubes with the

resection of the infected fundus of the uterus, leaving sufficient healthy uterine body to conserve the menstrual function and one or both ovaries to continue ovulation. The operation should be done without interfering with the ovarian circulation, hemostasis being secured by the ligation of the individual branches supplying the tube and fundus. With the bleeding controlled, a wedge-shaped excision is made of the upper part of the body and fundus of the uterus. The anterior incision begins just posterior to the insertion of the round ligament and runs across the front of the uterus to a corresponding point on the opposite side. The posterior incision begins between the tubal insertion and the ovarian ligament on one side and extends across the posterior surface to the same point on the opposite side. The incision is made in such a manner that the entire fundal mucosa with the pars interstitialis and surrounding tissues of both sides are excised. By means of this operation, sufficient endometrium is allowed to remain to perpetuate menstruation.

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## DISEASES OF THE LARYNX AND CONTIGUOUS STRUCTURES

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UNDER THE CHARGE OF  
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**Cyst of the Larynx.**—CHAMBERLIN (*Laryngoscope*, August, 1917) reports a case in a well-developed child who had had a peculiar cry almost from birth, shortly followed by inspiratory stridor which had become markedly worse during six months. There was no history of dyspnea or of cyanosis. The interior of the larynx could not be inspected with the aid of the laryngoscopic mirror, but under suspension a large tumor mass was seen to occupy the entire right side of the larynx, rendering a view of the interior impossible. An hypertrophied fold of mucous membrane at the summit of the left aryepiglottic fold flapped back and forth in the air stream, and accounted for the stertor. It was resected and the stertor ceased. A long knife inserted into the tumor with a view of determining its consistence gave exit to 1 or 2 drams of a brownish viscid, almost gelatinous liquid, and the tumor collapsed. Careful examination failing to reveal its walls or even the wound of the stab. It was thought that the tumor had been situated on the right aryepiglottic fold. An excellent and unobstructed view of the entire larynx and several rings of the trachea was at once possible. There had not been any recurrence of trouble up to the time of the report.

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**Excision under Suspension Laryngoscopy of a Carcinoma of the Larynx: No Recurrence in Three Years.**—MAYER (*Laryngoscope*, February, 1917) reports this case in which under suspension laryngoscopy he excised with long-handled, curved right and left scalpels a carcinomatous epiglottis which he exhibited at the New York Academy of Medicine. Save for a rather alarming hemorrhage on the second

day after the operation, an uninterrupted recovery ensued. The patient, a man, aged sixty-four years, had not experienced any discomfort whatever from the loss of his epiglottis, deglutition and vocalization being perfect.

**Diphtheritic Membranes in the Lung Diagnosed and Removed under Bronchoscopy.**—SKILLERN (*Laryngoscopy*, February, 1917) reports the case of a boy, aged seven years, supposed to have inspired a bead which accounted for existing cough and attacks of suffocation. Physical exploration of the chest and fluoroscopic examination were practically negative. Under bronchoscopic inspection there was detected, a little above and at the lower lobe bifurcation of the right lung, a membrane which bled on being loosened with a dull hook. It was not deemed prudent to continue manipulation at that moment. Two hours later dyspnea became so urgent as to require immediate tracheotomy. Three days later the membrane was loosened under bronchoscopy and on account of friability was found removable only piecemeal. Some pieces of membrane were coughed out through the cannula during the night. The tube was removed on the seventh day, the child being entirely well. Nine months previous to this clinical history the patient had gone through a severe attack of diphtheria followed for some two months by a cough which had cleared up entirely.

**Gunshot Wounds of the Larynx.**—COULET (*Revue de Laryngol., d'otol. et de rhinol.*, July 15, 1917) has found but one gunshot wound of the larynx among 1200 wounded soldiers under his care. He reports a case of gunshot wound of the larynx, followed by abscess and recurrent paralysis. A bullet from a great distance had passed through the neck without injuring the great vessels, but had injured the arytenoid region and induced local inflammatory action; and it had injured the recurrent nerve in passing. A good recovery ensued, but the paralysis of the left recurrent remained permanent.

**Chancre of the Pharyngeal Tonsil.**—HADEN (*Laryngoscope*, August, 1917) reports the case of a married woman, aged twenty-five years with headache unaccountable for by her eyes or her general condition. Though there had not been any history of trouble in nose or throat, posterior rhinoscopy, a swollen, bright red pharyngeal tonsil with apparent ulceration of its surface. Three days after an application of argyrol, though the pain became so severe as to require the administration of morphin, the patient expectorated a section of the pharyngeal tonsil which on microscopic inspection was found to contain numerous living *Spirochete pallida*. At this time a typical secondary rash appeared upon the body. Salvarsan was administered the next day, and the headache subsided.

**Septic Arthritis following Submucous Resection of the Nasal Septum.**—IMPERATORI (*Laryngoscope*, March, 1917) reports a case of septic arthritis of the knee-joint following resection of the nasal septum. Fluctuation was evident on the ninth day after the operation. The joint was opened and considerable pus was found with manifestations of extensive destruction of the articular cartilages.



**Saddle-nose Deformity after Submucous Resection of the Septum Corrected by Transplantation of Bone.**—CARTER (*Laryngoscope*, February, 1917) reports a case in which eighteen months after resection of the nasal septum, he corrected a resultant saddle-back deformity by transplanting about two inches of the ninth rib, working by the intra-nasal route. The deformity was completely corrected and the nose is as strong as it ever was.

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## PATHOLOGY AND BACTERIOLOGY

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UNDER THE CHARGE OF

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**Formation of Methemoglobin by Streptococcus Viridans.**—In the classification of the streptococci, constant use is made of the formation of methemoglobin upon blood agar by the organisms of the viridans group. This alteration of the blood pigment is readily distinguished, but the manner in which the bacteria act to cause this change is not very apparent. BLAKE (*Jour. Exper. Med.*, 1916, xxiv, 315) found that the change from oxyhemoglobin into methemoglobin took place only in the presence of the living microorganisms. The reaction appeared to depend upon the metabolic activity of the bacteria and had no relation to the virulence of the particular strain. The intensity of the activity bore some relation to the rapidity of multiplication. Hence it is found that the change in the hemoglobin was most marked when the medium contained the optimum of nutritive materials. Dextrose was one of the substances which enhanced the reaction. The results obtained by the author with the *Streptococcus viridans* are very similar to those reported by Cole for the pneumococcus. In both instances the reaction appears to depend upon processes of oxidation and reduction, for the result cannot be obtained in the absence of oxygen, while it is retarded when too much oxygen is present. There is no evidence that the change in the hemoglobin is due to a specific secretion on the part of the microorganism. The author points out that the results of the experiments suggest the manner in which bacteria may be injurious to other tissues by disturbances in oxidation because of the metabolic activities of the organism. This theory, it is suggested, is particularly applicable to the *Streptococcus viridans* because the lesions produced by it are prone to be localized and associated with the actual presence of the streptococci.

**Agglutination of *Treponema Pallidum* in Human Syphilis.**—Numerous attempts have been made to determine the presence of agglutinins in the sera of infected people or in experimental animals. Many of these studies failed to demonstrate agglutinins in sufficient quantity to make the test practical. On the other hand a few investigators believe that a technique is available whereby these specific substances can be recognized in the sera of infected individuals. KOLMER, BROADWELL and MATSUNAMI (*Jour. Exper. Med.*, 1916, xxiv, 333) using Zinsser's strain A of *Treponema pallidum* and a series of known sera obtained from patients with syphilis in different stages of the disease, studied the agglutinating properties by the macroscopic method. The sera were also controlled by careful Wassermann reactions. The control sera of normal individuals did not agglutinate the culture in dilutions of one in five or higher. But little evidence of specific agglutinins was found to appear in the blood during the primary lesion. On the other hand, 58 per cent. of the sera obtained in the secondary stage of syphilis showed definite agglutinins. Their presence became still more marked in tertiary and latent syphilis in which about 84 per cent. were positive. No direct relation between the presence of the Wassermann antibody and agglutinin was found. The former makes its appearance earlier and in higher concentration in all stages of syphilis. Strongly positive Wassermann sera may contain no demonstrable amount of agglutinin. The authors believe that the reaction for agglutinins may be made practical, but care must be taken in the choice of the culture for use in the test.

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## HYGIENE AND PUBLIC HEALTH

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UNDER THE CHARGE OF

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**Immunity to Trichinosis.**—SCHWARTZ (*Jour. Am. Med. Assn.*, September 15, 1917, p. 884) found that serum from animals convalescent from trichinosis when injected into other animals does not produce immunity to trichinosis in the latter. Trichinous meat mixed with serum from animals during the active or convalescent stage of the disease proved to be still capable of producing the disease. Animals once infected and harboring trichinae in their muscles are not immune to further infection when fed trichinous meat. Serum from a trichinous animal has no observable ill effects on the larvae freed from their cysts by artificial digestion.

**Malaria.**—TRASK (*Public Health Reports*, December 22, 1916) states that in the territory extending from the Gulf of Mexico to a line north of the Ohio River and from the Atlantic seaboard to and into the eastern part of Kansas, Oklahoma, and Texas, few, if any, localities are entirely free from malaria. In most of the lowlands, it is very prevalent; in the mountains and better-drained areas less prevalent. The disease is also endemic in southeastern New York and parts of Connecticut, Rhode Island, and Massachusetts, and in California in the Sacramento and San Joaquin Valleys. There is probably no State in the Union in which the disease is not present and in which it is not spread by mosquitoes grown locally. The disease constitutes one of the big national health problems. It is also an economic problem of importance. The actual geographical distribution of the disease and its relative prevalence can be definitely determined only by making painstaking malarial surveys or by requiring cases to be reported to the health authorities and the authenticity of the reports verified by blood examinations.

**Immunization against Typhus Fever.**—MCCOY and NEILL (*Public Health Reports*, June 1, 1917, p. 841) made studies to determine whether it is possible to immunize monkeys against typhus fever by means of a vaccine made from the Plotz bacillus (*B. typhi exanthematici*). The negative results obtained from these studies plainly show that monkeys cannot be thus protected against typhus fever in this way. These results also throw doubt upon the etiological relationship between the Plotz bacillus and typhus fever.

**Dog Disease Nambi-uvu and its Parasite, Rangelia Vitalii.**—CARINI (*Zentralbl. Bakt.*, 1916, Part 1, p. 265) states that the disease is prevalent in Brazil particularly among hunting dogs. The name Nambi-uvu means "bleeding ear" and it is derived from the fact that bleeding from the ear is a very prominent symptom. The disease is also associated with icterus and therefore often called the "yellow fever" of dogs. Another name is "blood plague" (*peste de sangue*). The causative parasite has first been described by B. R. Pestana in 1910 (*Rev. med. de Sao Paulo*, 1910, p. 423). The disease prevails during the entire year but it is most frequent during the summer. The author describes the symptoms, diagnosis, pathology, and etiology of the disease at some length. The disease is pathogenic to dogs only and newborn dogs are particularly susceptible. The acute form is the icteric, the subacute the hemorrhagic type. There is also a chronic mild type. The parasite is found in the blood. The blood of recovered animals remains infective. The mode of transmission from dog to dog is unknown. It is possible that ticks are responsible. The article contains illustrations of the life cycle of the parasite in the blood.

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THEODORE CALDWELL JANEWAY, A.M., M.D.

## THEODORE CALDWELL JANEWAY, A.M., M.D.

THEODORE CALDWELL JANEWAY was born in New York City on November 2, 1872, and died in Baltimore on December 27, 1917, in the forty-sixth year of his age. He was the son of Edward Gamaliel Janeway, the celebrated physician. These men served two succeeding generations with surpassing fidelity. The elder Janeway was a silent, studious, keenly observant man, with a heart full of the kindest spirit. He was one of the physicians of the old-fashioned school to whom the sense of having been of service to a family in trouble was of far greater significance than any other reward. At a dinner given to Theodore Janeway by his friends in New York just before his removal to Baltimore, he spoke beautifully of his father's influence upon him, of the injunction repeated from his childhood, "You are to be a physician," and of his deep-seated sense of obligation that since he was the son of such a father he must be a good physician.

Theodore Janeway was graduated from the Sheffield Scientific School in 1892. He had there come under the influence of Chittenden. He graduated from the College of Physicians and Surgeons, Columbia University, in 1895, and later served as intern at St. Luke's Hospital. At the time of the reorganization of the New York University and Bellevue Hospital Medical College, in 1898, of which institution his father was Dean, he became instructor and then lecturer on medical diagnosis, which position he filled until 1905. He also worked in his father's office and had the opportunity of seeing the rare and puzzling diseases which passed through his father's hands. He was the first instructor in medicine in New York City to attempt to teach the subject from the stand-point of disease being a deviation from the physiological normal; he wrote a book on the subject of blood-pressure, and designed the first satisfactory apparatus for the clinical determi-

nation of the blood-pressure at the bedside. His reports to the faculty concerning the reorganization of the dispensary, of which he had charge, were models of their kind. The discouragements encountered at this time can scarcely be appreciated by the medical student of the present day. He knew how his father had fought for better hospital conditions and had failed to effect any betterment. It is, perhaps, not yet time to write of the difficulties of his life at this period, or of the failure of some of the older men of the college with which he was associated to correctly read the future trend of medicine in this country or to appreciate the ability of this brilliantly endowed young man. The conditions were such as to cause him to resign from the college.

Continuing in his father's office, he also became visiting physician to the City Hospital, of which at that time his friend Dr. Horst Oertel was pathologist. Here he gave optional clinics to the students of the College of Physicians and Surgeons, illustrating them with the demonstration of pathological material, after the manner of the great teaching clinics of the Old World. His success was marked, in 1907, by the endowment of the pathological work by Mrs. Russell Sage in her creation of the Russell Sage Institute of Pathology and by his appointment as associate professor of medicine at Columbia. This appointment was quickly followed by his elevation to the Bard Professorship of Medicine in 1909. This was frankly because he, at the age of thirty-seven, had no equal in this country. He worked at this time without sparing himself. Laboratory, teaching, the reorganization of the great Presbyterian Hospital along modern lines, as well as a private practice, made the burden so great that his health broke down in 1914 and he was obliged to pause and rest.

In 1914 another great decision presented itself. He was asked to become a "full-time" professor of medicine at the Johns Hopkins Medical School, to take the chair previously held by Osler, but under new conditions. These were that all fees derived from private practice were to be turned over to the hospital and that an academic salary was to be the only recompense. In discussing the matter with the writer previous to his decision, he said he was sure his father would have told him to take the position. Here it required a leader of men to fill the place, but it required above all a conscientious fealty to what is best in life to make the

decision. He moved to Baltimore and remained there until his untimely death from pneumonia on December 27, 1917. During recent months he had been serving under General Gorgas as major in the United States Army. He was director of research on the subject of heart disease among the soldiers, his own extensive researches into such conditions making him the natural leader in these efforts. He was as much a sacrifice to his country as though he had perished on the battlefield. As he had done when a younger man, he would work until tired out and then work three hours longer. He burned himself out in devotion to duty, and, by the dedication of his life to the altruistic service of mankind, accomplished in the short span of forty-five years a marvelous amount of good work. He overcame the powerful opposition to proper hospital reorganization in New York and gave to students the stimulating incentive only to be conferred by a real master of medicine. His own opinions of hospital reorganization he thus expressed in 1912:

"A medical clinic such as has been outlined could undertake the whole instruction in medicine of from 100 to 120 students. An analysis of its organization shows at once that it is the British or Scottish teaching hospital surmounted by a German university clinic. Our American hospitals were the direct outgrowth of their British predecessors, but they had to be cramped and modified to meet conditions originally provincial; now, in our large cosmopolitan cities, they are rapidly returning to their original lines. It does no violence to tradition therefore to integrate them into a great university medical school and to add to them that coördinating activity of a clinical master which shall develop their latent possibilities of larger educational usefulness and permeate them with that atmosphere of tireless scientific investigation which Americans seek in Germany today. Is it too much to hope that, with American energy and open-handed American generosity at our disposal, the talent for organization—which has been so marked a feature of our contemporary industrial life—may in the next generation make of our American medical clinics institutions for the treatment of the sick, sought alike by poor and rich, and centers of instruction for the world?"

Shortly after this was written came the happy days spent in London, in 1913, at the last International Medical Congress, at



which both he and Friedrich von Müller, of Munich, were among the guests of Osler at Brown's Hotel, days which had little warning that the Spirit of Evil would obtain dominion over the minds of those who caused the war.

Many competent to judge agree that the loss of Janeway is the greatest that medicine in this country could have suffered.

Slight in frame, nervous in temperament, but never irritable, speaking quickly and easily, fond of wit and merriment, interested in all forms of charity and public benefit, devoted and generous to his friends, charitable to those whose actions clashed with his ideals, he fought a good fight and lived to see the triumph of his principles.

In 1898 he married Eleanor Alderson, who steadfastly upheld him in the struggles that beset his life. He also is survived by his mother, Mrs. E. G. Janeway, and five children, Eleanor A., Edward G., Agnes, Charles A., and Francesea.

GRAHAM LUSK.

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ORIGINAL ARTICLES

THE PATHOLOGICAL UTERUS AT THE MENOPAUSE.

BY CHARLES R. ROBINS, M.D.,

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CIRCLE HOSPITAL, AND GYNECOLOGIST TO MEMORIAL HOSPITAL, RICHMOND, VA.

IN looking over a series of cases recently in which I performed the operation of hysterectomy, I find that 58 occurred in women who were forty years old and over, and in all of these the complete removal of the uterus and adnexa had been practised. In 28 of these the operation was performed for fibroids, pelvic inflammation and other conditions in which the impossibility of conserving the organs was manifest and beyond dispute. In the remaining 30 cancer was either a positive or a possible diagnosis. In 4 a positive diagnosis of cancer of the cervix, afterward confirmed by the microscope, was made and a Wertheim operation, preceded by cauterization with the Percy cautery, was done. In 26 a diagnosis of chronic metritis, including in this induration of the cervix, was made and a possibility of malignancy considered. In practically all of these bleeding from the uterus was a prominent symptom, manifesting itself as irregular or continuous bleeding, and sometimes accompanied by marked anemia. In 2 cancer of the fundus was found on opening up the uterus.

In attempting to arrive at the diagnosis of cancer of the uterus we are often met with great difficulties when the case is in its incipency and therefore presenting the best hope from an operation. In advanced cases, with marked symptomatology and gross pathological involvement, the question of diagnosis does not present itself, it is obvious, and with these cases we are not concerned at this time.

Usually when the cancer is situated on the vaginal aspect of the cervix it can be diagnosed in its earliest stages by physical examination, but in cases originating in the cervical canal or the fundus an early diagnosis without the microscope must remain a conjecture.

If we consider the symptoms associated with cancer which we could reasonably look upon as danger signals we are painfully impressed with their uncertainty and irregularity. The most commonly accepted and most reliable is an atypical bleeding. This may manifest itself as a slight show following some form of trauma, as coition or straining at stool, a bleeding between periods or excessive bleeding at periods or a bleeding returning after the menopause. The principle point in all of these is the development of a bleeding which has not previously existed and which does not present an obvious etiology. However, we can recall cases in which the most careful questioning failed to elicit a history of any type of bleeding in the early stages of the disease, and the first symptoms were those of pain from extension of the disease into the parametrial tissues. Still further uncertainty is produced by the fact that such symptoms may be occasioned by other conditions than cancer, particularly hyperplastic endometritis, which frequently springs up about the time of the menopause, and the development of a small fibroid polypus in the fundus. The indurated and enlarged cervix of chronic cervicitis also is quite difficult to diagnose from the induration and reaction present in cancer of the cervical canal. In addition to this it is now being generally admitted that any pathology of the cervix or fundus may be regarded as a precancerous condition and that the transition into malignancy may be so insidious as to present no special symptomatology until carcinoma is well advanced. In fibroids, for instance, we may have malignancy engrafted when an examination may show only the benign condition, which apparently fully accounts for the symptomatology present. It would thus appear, and is generally conceded, that unless the growth comes under the eye or direct touch that it is practically impossible to accurately diagnose a beginning malignant condition, and even then a microscopic examination may be necessary.

For the purpose of securing tissue for microscopic examination we have recourse to two methods, curettement when the growth is suspected in the body of the uterus and excision of a portion of the cervix when it is suspected. Both of these are open to serious objections. A curettement must be complete in order to be conclusive, and unfortunately it is often not as complete as we think it is, so that it is possible to secure a negative report even when the cancer is present. Excision of a portion of the cervix is open to the same objection, that we might not get just exactly the tissue that is involved. Again, in both of these cases, if satisfactory work is done, anesthesia is necessary, which unless frozen section is used means a second anesthesia. But above all I am convinced that cutting into cancer at all is bad technic and undoubtedly causes invasion of sound

tissue by cancer cells. This is particularly true if an appreciable time elapses before the final operation is done. This is obviated to some extent by the use of frozen section with immediate operation, but even then I believe that it is dangerous. How many minutes or how many days it takes for these cells to invade we have no means of ascertaining.

It has been suggested that in view of the uncertainties of diagnosis by means of curettement and excision of tissue that the cervix should be amputated and the uterus opened through an abdominal opening for complete examination and inspection. While this would make the diagnosis much more exact it would amount to preliminary operation, and where it is to be followed by a total hysterectomy it would certainly add an appreciable risk. In the same length of time the uterus could be removed.

Taking all of these things into consideration I have come to the following conclusions and have made them my basis of practice for some years:

1. In cases favorable for cure from operation it is not always possible to make an exact diagnosis.

2. In our efforts to make our diagnosis exact we are liable to lose the advantage of an early operation by our efforts to secure tissue for examination, in this way disseminating cells and stimulating vicious growth.

3. That a pathological uterus is potentially a malignant one, and that even if cancer is not already present it may develop later.

I therefore believe that the line of safety requires that in those cases occurring in women about the menopause or after, where the symptoms and physical findings would suggest the possibility of malignancy, that our procedure should be a total extirpation of the pelvic organs and the pathological investigation made after the organs have been removed. In 26 such cases cancer was found in 2, or slightly less than 8 per cent.

These conclusions are based on the consideration of malignancy alone, but there are other very excellent reasons for removing such uteri. In the first place they are pathological and have produced enough symptomatology to cause the patient to consult the physician. The pathology has usually existed for a long period of time and the alterations have become so permanent that conservative measures are liable to be disappointing in results.

The organs have fulfilled their usefulness and under normal conditions would be obliterated by nature. We are therefore simply acting in the line of nature when a removal is practised.

Our efforts to conserve often require multiple and time-consuming operations, and the net result of our efforts are to save something that the patient is better off without.

In certain types of bleeding uteri, conservative measures do not relieve. I have had cases of hyperplastic endometritis that have persisted over periods of years, and which have been curetted

repeatedly, with only the most temporary relief, the hyperplasia returning promptly after each curettement. In other cases where the bleeding has been sufficient to keep the hemoglobin under fifty for long periods, examination of the uterus has shown no pathology of the mucous membrane or any tumor formation or any change in the uterus other than slight increase in size and thickening of the wall. I have not found that curettement is of much benefit in relieving the excessive bleeding that so often occurs about the menopause.

When we encounter a pathological uterus at the time of the menopause the first question should be, "Why save the uterus?" The burden of proof is to show why it should be saved. My own opinion is that when such cases present themselves and the symptomatology is completely accounted for by an obvious pathology which can be easily corrected, that this is all that is necessary. On the other hand, when the pathology is gross, particularly when the uterus is enlarged or the cervix indurated or both, and especially when irregular bleeding or debilitating hemorrhages are present, that the most conservative treatment, so far as the present and future welfare of the patient is concerned, is total ablation of the pelvic organs.

In this connection we have to consider two points, mortality and effect of operation on patient. In reference to mortality I have found the radical operation safer than a series of conservative operations. The group of cases considered in this paper is too small to furnish a basis for mortality statistics, but there were no deaths.

As to the after-effects on the patients I have been able to observe no bad results. We have to remember that nature is about to obliterate these organs and their function is over, and in addition they have been the source of impaired health for a more or less prolonged period. My experience has been that the patients improve in health and strength and pass from a state of semi-invalidism, with a tendency to introspection and pessimism, to a cheerful, happy existence in which they are able to take their share in the various activities of life.

In order to secure good results after hysterectomy, however, the technic must be clean and devoid of trauma and the parts left properly supported by attachment of ligaments. While the operation can be quickly done, technic should not be sacrificed to time, and often small details have an immense effect on the future welfare and usefulness of the patient.

I believe that we may fairly conclude the following:

Total abdominal hysterectomy is the operation of election in the pathological uterus at the menopause.

In an appreciable number of such cases cancer will have been found to have already developed.

The adoption of radical methods in dealing with such cases offers the surest protection to women from cancer.

A CONTRIBUTION TO THE NATURE OF THE MONONUCLEAR  
CELLS SEEN IN THE EXUDATE OF LOBAR PNEU-  
MONIA ACCOMPANYING TYPHOID FEVER.

BY JONATHAN FORMAN, M.D.,

AND

C. CLARON HUGGER, M.D.,

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IN his histological study of typhoid fever Mallory<sup>1</sup> describes the exudation seen in a lung of a case complicated by a typical fibrinous pneumonia of the whole lower lobe in the stage of a gray hepatization. In his specimen a very few pneumococci were present, while a bacillus, morphologically like the typhoid bacillus, occurred more abundantly, and usually within the leukocytes. In the exudate were great numbers of "large phagocytic cells with irregular vesicular nuclei situated peripherally." These cells had ingested both polymorphonuclear leukocytes and red blood corpuscles. Mallory feels that these cells are endothelial leukocytes, for he observed no evidence of migration on the part of these cells. He further observed many mitotic figures in large cells seen in the alveoli. These, of course, might be epithelial as well as endothelial, but Mallory believed after his study of the primary lesions of typhoid fever that it was not unreasonable to assign the same origin to these as that of the other mononuclear phagocytes, *i. e.*, endothelium.

Pratt<sup>2</sup> found that many of the mononuclears in early pneumonia resembled closely the cells seen in the blood and classified as "transitionals." He observed some of these same cells in the blood stream. In spite of the fact that there was not an increase of these cells in the blood stream, he felt that the "transitional" cell did enter into the formation of the exudation of early lobar pneumonia.

Evans<sup>3</sup> approached the problem of the cytology of this exudation in a different manner. He studied, by means of the indophenol blue synthesis, three specimens of lobar pneumonia which came to necropsy on the third, fourth, and fifth days of their disease respectively, together with that found in the early stages of experimental pneumonia in rabbits. Of the mononuclear cells seen in this exudate he described and classified as follows: "(1) A few typical lymphocytes. (2) A few desquamated alveolar wall epithelial cells. (3) Relatively many oxydase-containing, large mononuclears of the blood belonging to the so-called transitional-cell group of Naegeli.

<sup>1</sup> An Histological Study of Typhoid Fever, Jour. Exper. Med., 1898, iii, 632.

<sup>2</sup> Histology of Acute Lobar Pneumonia, Johns Hopkins Hosp. Reports, ix, 265.

<sup>3</sup> Evans, F. A.: The Cytology of the Exudate in the Early Stages of Experimental Pneumonia, Jour. Infect. Dis., 1916, xix, 440. Experimental Study of the Mononuclear Cells of the Blood and Tissues, Arch. Int. Med., 1916, xviii, 692.

(4) Almost as many non-oxydase-containing, large mononuclears of the blood or closely related forms." Further, the injury of the leukopoietic organs by means of benzol resulted in a loss of cells in the exudation when a pneumonia was induced, although the histogenous macrophages had been spared. In the exudation in pneumonia induced in rabbits heavily stained by combined intravenous and intraperitoneal injections of lithium carmine, neither the oxydase nor the non-oxydase mononuclears contained the vital stain.<sup>4</sup>

Winkler, Scultze, Gierke and others have applied the indophenol blue synthesis of Ehrlich as a differential test for the recognition of cells of myeloid origin in tissues after formalin fixation. For this purpose the test has become widely recognized. It has been used by Evans upon blood smears (1 and 2) and upon exudates in his studies of the mononuclear leukocytes (3 and 4) and of the reaction of the spleen to acute infections.<sup>5</sup> Forman and Warren<sup>6</sup> have used it in the identification of the cell types in myelomas. For a review of the literature and a description of the technic of the application of this reaction the reader is referred to the papers by Evans. In the light of the observations cited above, a study of the cytology of the exudate in a pneumonia associated with typhoid fever by means of this reaction should prove of interest.

Lobar pneumonia accompanying typhoid infection is not of frequent occurrence, and is usually due to some secondary infection. This is a study of such a pneumonia occurring in a young man, aged twenty years. There was an involvement of the lower lobes of both lungs, which for the most part were in the stage of gray hepatization.

The specimen had been preserved in 10 per cent. formalin for about two years and a half. According to Evans, tissues over a year old have been said to give the indophenol reaction. Graham,<sup>7</sup> with a decidedly modified technic, has been able to demonstrate peroxidase ferments in tissue preserved for six years. It therefore became necessary to investigate further the length of preservation of indophenol oxydase granules by formalin. The test was applied to sections from specimens of lobar pneumonia in the stage of gray hepatization which had been kept in 10 per cent. formalin several years under the same conditions as the specimens from the typhoid case under consideration. The oldest of these specimens had been preserved for six and a half years. The polymorphonuclear leukocytes in all these specimens contained the characteristic number of indophenol oxydase granules.

<sup>4</sup> Observations on the Origin and Status of the So-called Transitional White Blood Cell, *Arch. Int. Med.*, 1916, xvii, 1. The Practical Significance of the Oxydase Refraction as Applied to Blood Cells, *Proc. New York Path. Soc.*, xv, 144.

<sup>5</sup> Evans, F. A.: Spleen in Acute Infections, *Bull. Johns Hopkins Hosp.*, December, 1916, p. 356.

<sup>6</sup> The Identification of the Cells Seen in Myelomas by Means of the Indophenol Blue Synthesis, *Jour. Can. Res.*, 1917, ii, 79.

<sup>7</sup> The Oxidizing Ferment of the Myelocytic Series of Cells and its Demonstration by Alpha-naphtholpyronin Method, *Jour. Med. Research*, November, 1916, p. 231.

Unfortunately, cultures were not obtained from the lungs at the time of the autopsy. Microscopically, however, very many bacilli were present in the sections from the pneumonic areas. These resembled closely the typhoid bacillus. Rarely coccoid forms usually arranged in pairs were encountered. While no doubt other organisms were aiding in the production of the pneumonia, the reaction has been definitely influenced by the presence of the typhoid infection in the individual, and, judged by the description and drawings, is quite similar in its cytology with the case described by Mallory.

A few areas of congestion and those containing a typical fibrinous exudation were encountered, but for the most part the alveoli were filled with serum and an abundance of cells. Many of these cells were polymorphonuclear leukocytes, and in some alveoli this type of cell predominated, a few were lymphocytes, and there was an occasional plasma cell. The predominating cells, however, were large mononuclear phagocytes. Relatively a few of these cells were much larger than the others, and frequently contained particles of black and brownish pigment. From their size, morphology, and the fact that no indophenol oxydase granules were observed in them it was assumed that they were epithelial cells. The remainder of the mononuclears resembled each other in size and shape very much. The greater number of these cells contained indophenol oxydase granules. The others, however, did not. The granule-containing cells usually possessed slightly or distinctly indented and eccentrically placed nuclei. These cells had ingested many red blood corpuscles and to a less extent polymorphonuclear leukocytes. The cells of the other group of mononuclears, which did not give the oxydase reaction, were not so numerous, and apparently they presented more frequently a round or oval nucleus. Cells of this group, however, were observed with irregular nuclei.

That some of these cells may be of lymphoid origin seems probable, and, on the other hand, it does not seem unreasonable to assume, as Mallory did, that some of them are of reticulo-endothelial origin.

In this connection an observation of Graham is of interest. With his alpha-naphthol—hydrogen peroxide—pyronin technique he has noted "that the endothelial cells of the hepatic sinusoids contain larger and smaller bodies that give a typical enzymic reaction." He also observes "that in blood smears occasional cells are found that have all the appearance of the endothelial leukocytes, so-called 'large mononuclear' or 'transitional' cells, but contain a few granules reacting to the alpha-naphthol reagent." Occasionally, in the exudate in our specimen, large mononuclear cells were encountered which tend to confirm Graham's observations. A cell with an oval nucleus has been seen in whose cell body was the nucleus of an ingested polynuclear leukocyte. The cytoplasm of this cell stained a diffuse blue without the presence of definite granules. Again, cells of the same type were encountered in which only a few granules



could be seen. The suggestion of Graham seems probable that such a result is due to phagocytosis, since Winkler has shown that the leukocytic granules resist the action of ptyalin, pepsin, and trypsin even after the remainder of the cell has been broken down.

While such an explanation accounts for a certain number of these mononuclears giving an apparently positive reaction to the indophenol blue synthesis, it does not account for the great number of cells which contain an abundance of oxydase granules. These are of myeloid origin, and, like the cells seen by Pratt and Evans, are best considered as belonging to the so-called transitional-cell group. Another observation which also strengthens this view is that in the lumina of bloodvessels of this lung similar oxydase-containing mononuclears can be found.

We have here a lung in the stage of gray hepatization with an exudation almost identical in its cytology with that seen by Evans. Whether this type of exudation has been continued through the course of the pneumonia due to specific stimulation of the "transitional-cell group" or whether it is due to the stimulation by a superimposed pyogenic infection of injured leukopoietic tissues is not entirely clear. Since, however, the bone marrow in typhoid fever shows definite lesions and the production of granular myelocytes is held in abeyance the last explanation would appear the more probable.

**SUMMARY.** It would appear that in the exudation in lobar pneumonia accompanying typhoid fever the mononuclear cells predominate. These mononuclear cells may be classified as: (1) lymphoid cells; (2) epithelial cells which have desquamated into the air sac; (3) large mononuclear leukocytes in abundance which contain indophenol oxydase granules; (4) large mononuclear leukocytes which are not so numerous and which do not contain the granules reacting to the indophenol blue synthesis.

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### UNSUSPECTED SYPHILIS: A STATISTICAL STUDY.

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THE object of this paper is to present certain statistical data drawn from the Wassermann reaction as applied to 567 consecutive private patients. Most of these patients were of the well-to-do classes, and all of them were seen in consultation, which fact warrants the assumption that they exhibited, as a whole, the more serious or puzzling diseases of inner medicine. None were supposed to suffer with venereal disease.

The Wassermann tests were done by Miss Blanche Frazier, whose

training has been thorough and long, and every detail which could make for accuracy has been painstakingly studied. The original Wassermann technic, done in half-quantities, was employed, using as antigens alcoholic extracts of both human and beef heart, and an antishoop hemolytic system, adding two full units of complement to all tests together with preliminary ice-box incubation for four hours at 8° C., and final water-bath incubation for one-half hour at 37° C.

Of these 567 consecutive patients, 94, or 16.5 per cent., gave a positive Wassermann reaction; 7, with a negative Wassermann reaction, showed unmistakable clinical evidence of syphilis, thus bringing the known percentage of this disease to 17.8. These figures, then, represent a legitimate estimate of the frequency of syphilis in the better class of patients who suffer with the more obscure or serious medical syndrome.

The anamnesis as regards syphilis is proverbially unreliable. The fact, however, that the patients of whom I write were above the average in intelligence, and in a desire to cooperate, lends additional interest to their histories. Among the 94 individuals whose Wassermann reactions were positive, only 27, or 29 per cent., admitted a venereal ulcer or other evidence of syphilis. It is startling to note that of this number 21 believed themselves cured, most of them basing their belief upon a physician's advice.

Another group of 9, while categorically denying syphilis, gave histories which to the initiated pointed unmistakably to such an infection. Adding these 9 to those who admitted an infection we have 36 patients, or 38 per cent., whose histories pointed with reasonable certainty to syphilis. The remaining 58 (62 per cent. of the entire Wassermann positive group) gave no such history, direct or suggestive.

It is interesting to inquire further into these 58 "Wassermann-positive, history-negative" cases. Six on being confronted with a positive Wassermann reaction then recalled a long-forgotten venereal ulcer. The knowledge gained from a positive Wassermann reaction led always to renewed delving into family and past histories, and in 8 instances syphilis was thus found in husband, wife, or parent. Without the stimulating guidance of a known positive Wassermann reaction this information would have been lost.

There were 10 others of this group who presented clinical evidence which, apart from the serum reaction, would alone point to syphilis. This included 4 instances of aortic aneurysm, 1 of aortitis, 5 of characteristic skin or throat lesions, 1 of a paroxysmal hemoglobinuria, 1 of characteristic neuroretinitis, and 1 of typical cerebrospinal fluid changes.

Turning now to a consideration of the influence of syphilis upon the several internal organs, the heart and the aorta here, as always, are entitled to first place. It is difficult to differentiate invariably between essential myocardial disease, cardiorenal disease, and

simple hypertension. In this series were 30 patients with essential myocardial disease, of whom 14, or 45 per cent., gave a positive Wassermann reaction.

Four of the five patients with aortic aneurysm gave a positive Wassermann reaction.

The arterial hypertension group presents a rather heterogeneous lot, for I have included here those with and without demonstrable arteriosclerosis as well as those with and without obvious kidney disease. There were 65 such patients, and 15, or 23 per cent., gave a positive Wassermann reaction.

There were 26 patients who gave roentgenological and other evidence of ulcer of the stomach or duodenum; 8 gave a positive Wassermann reaction, and 5 of these, under the influence of salvarsan as well as dietetic and other measures, have apparently recovered.

Of 28 patients with pulmonary disease, apparently tubercular, 6 gave a positive Wassermann reaction, and of these 6 only 2 showed tubercle bacilli in their sputum; 5 were given antitubercular treatment, all of whom have experienced satisfactory improvement or cure, but since all had the benefit of the usual hygienic measures, conclusions are difficult. Observation of the roentgenological signs and the clinical course in one of the patients at least, tempts me to state unreservedly that we were dealing with syphilis alone.

The diagnosis of neurasthenia which was given 61 patients needs no defence except the statement that in this group of emotionally unbalanced individuals were placed numerous unfortunates whose disabilities no doubt rested upon the widest variety of unrelated causes. Varicolored perhaps as to morbid processes the group, as a whole, presents a familiar and rather clearly defined clinical entity. Of the 61 neurasthenics 23, or 32 per cent., gave positive Wassermann reactions. In only 1 of these did the spinal fluid suggest organic nervous disease.

While syphilis is known to be an occasional cause of obscure low-grade fever, I have never heard discussed the influence of latent syphilis in causing the continuance of a fever initiated by some other infectious process. There were 2 cases of typhoid fever and 1 of pneumonia, in each of which slight continued elevation of temperature persisted long after the original infection seemed to have subsided. In each of these the Wassermann reaction was positive and the fever promptly disappeared when appropriate treatment was given.

One patient deserves special mention: A physician, whose history was almost identical with that of Fordyce's male nurse, consulted me because of an eruption on his own person which a skin consultant recognized as syphilis. The Wassermann reaction was positive. Eight weeks previously, in giving salvarsan to a patient with florid syphilis, this man had accidentally punctured his own finger and spilled the patient's blood upon his hand which he sought to remove

with a stiff brush. This instance he tells me, and I credit fully his statement, was his only opportunity for acquiring syphilis. No ulcer appeared at the site of the puncture or elsewhere, and a careful but unsuccessful search was made for a scar or discoloration which might give evidence of syphilis otherwise acquired. I am satisfied that his infection occurred as related and without the production of an initial lesion.

The routine use of the Wassermann reaction in private work as well as in the clinic to me has eminently justified itself. It has told of the startling frequency of syphilis in the innocent as well as the guilty, and has clarified many a perplexing clinical problem.

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### SPIRAL FRACTURES OF THE TIBIA.

BY CHARLES DAVISON, M.D.,

CHICAGO.

SPIRAL fractures of the tibia are produced by torsion and bending of the leg, and are always accompanied by fractures of the fibula. Spiral fractures are more common in the tibia than in any other bone, constituting fully one-seventh of all fractures of the shaft of the tibia. Adult males are more subject to this injury, probably because of their more hazardous occupations.

The mechanism of these injuries shows that they are the result of indirect violence. A man missteps with one foot or slips on the ice or a banana peel, the other foot remaining fixed in contact with the ground. As his body turns and he struggles to regain his equilibrium, his whole weight is thrown upon one leg. The rotation of the body upon the leg with the foot fixed furnishes a torsion force of the type which produces spiral fractures of the tibia.

In whatever manner the leg may be subjected to a twisting and bending force of sufficient intensity, the tibia, which is the substantial weight-bearing bone of the leg, breaks at the location of least resistance and greatest strain. These fractures uniformly occur at the region of the junction of the middle and lower thirds of the tibia. This is the place of least resistance and greatest torsion strain, because of the size, shape and character of that part of the bone. At this location the bone is smaller and more nearly cylindrical than elsewhere, and the compact bone is extremely dense and inelastic.

The spiral fracture in the tibia is accompanied by a fracture of the fibula, usually impacted in rotation. The fibula is broken in its upper part in the line corresponding to the torsion force. If the direction of the spiral of the fracture in the tibia is followed upward a characteristic injury will be found in the fibula. This injury will be at a very definite location in the fibula, depending upon the angle of the axis of the spiral in the fracture of the tibia to

the shaft of the tibia. The axis of the spiral extended until it reaches the fibula, locates the break in the fibula.

The mechanism of the fracture in the fibula is that of indirect violence. When the tibia breaks the weight of the body and the torsion force are transferred to the fibula, and that bone breaks at a higher level, depending upon the length and direction of the spiral in the tibial fracture. The fragments of the fibula are nearly always impacted. The lower fragment is rotated to correspond to the rotation displacement of the lower fragment of the tibia. This impaction is important, as when it persists it prevents reduction of the fracture in the tibia.

The deformity produced by spiral fracture of the tibia, with impacted fracture of the fibula, as shown by the roentgenogram, is characteristic. The spiral of the fracture in the tibia curves from above downward, forward and outward. The impacted fracture in the fibula is high up, in line with the spiral of the tibial fracture, and the lower fragment is in external rotation. There is 1 cm. to 3 cm. overriding of the tibial fragments, depending upon the amount of impaction of the fibular fragments. The lower fragments of the tibia and fibula retain their normal relationship to each other. The fragments of the tibia have little contact. The amount of separation depends upon the amount of rotation in the impaction of the fragments of the fibula (Fig. 13).

Reduction of spiral fractures of the tibia by external manipulation and extension is not possible while the impaction of the fragments of the fibula remains. Even when the fragments of the fibula are liberated from impaction it is usually impossible to reduce the fracture in the tibia because of the entanglement of the upper end of the lower fragment of the fibula.

Treatment by external manipulation and external immobilization results in good union of the fibula in the impacted position, but in the majority of cases in only partial union, weak union or non-union of the tibia—the strong weight-bearing bone of the leg—in the position of the original deformity. The amount of osseous union often consists in only a slight bony bridge between the displaced fragments. Even a large amount of callus may fail to connect and fix the ends of the fragments (Figs. 1, 2 and 3).

Open operation with surgical fracture of the fibula at the same level as the fracture in the tibia is usually necessary to mobilize the lower fragment of the tibia before reduction can be accomplished. When reduction has been satisfactorily accomplished the fragments of the tibia can rarely be immobilized so that they will remain in position except by the aid of internal fixation, because of the spiral shape of the fractured surfaces.

Internal fixation in these fractures may be best accomplished by the transplantation of bone, by the grafting across the line of fracture, in the medullary canal, of a splint of fresh live bone from

the same individual. This furnishes a method of alignment and fixation by a living, germ-resisting, osteogenic structure, which is treated kindly by the tissues and which heals in as an integral part of the body.

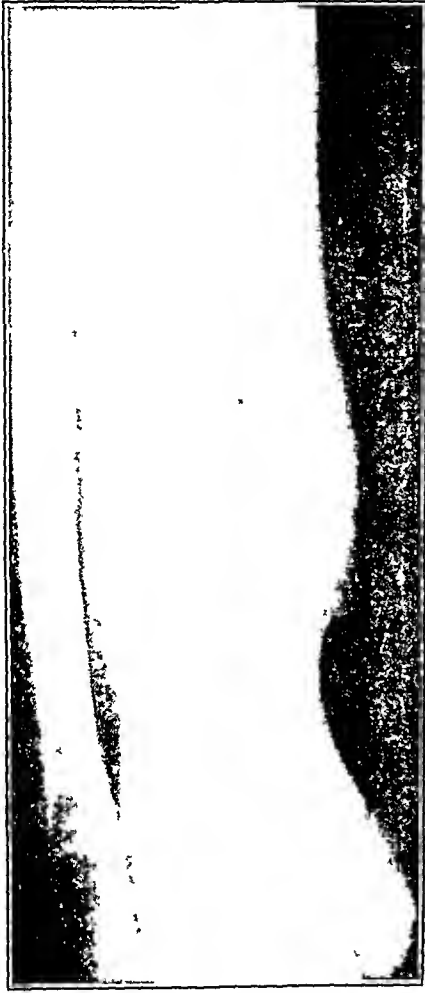


FIG. 1.—Roentgenogram of a spiral fracture of the tibia, with an impacted fracture of the fibula, treated by external manipulation and external immobilization, showing non-union of the fracture in the tibia one year after injury.

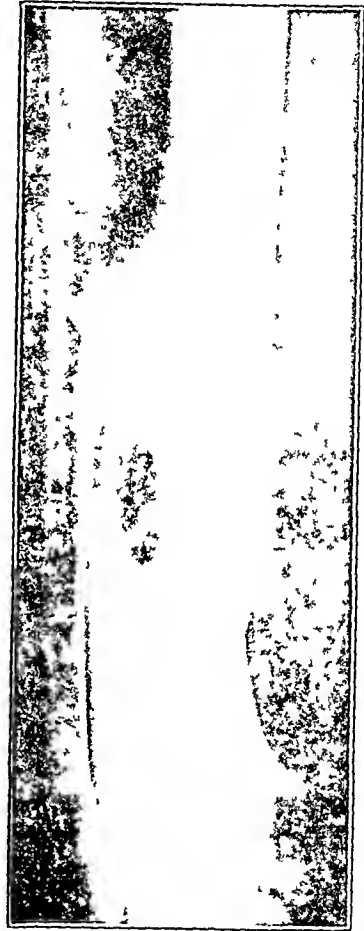


FIG. 2 —Roentgenogram of a spiral fracture of the tibia, with an impacted fracture of the fibula, treated by external manipulation and external immobilization, showing a large amount of callus, but failure of weight-bearing union.

The transplant aligns the fragments, stimulates osteogenesis at the injury, lives and grafts to the compact bone of each fragment, when actual contact has occurred between the transplant, from which the periosteum has been removed, and the compact bone of each fragment and when the limb has been properly immobilized by external means, so that there can be no movement between the transplant and its host.

Under these favorable conditions the transplant becomes a living integral portion of the repaired bone, taking its part in the functional



FIG. 3.—*a*, roentgenogram of spiral fracture of the tibia treated by external manipulation, followed by nail-extension with twenty pounds of weight for three weeks, without change of position of the fragments; *b*, roentgenogram of impacted, rotated fracture of the fibula which prevented reduction.

support of the extremity and maintaining for the time its shape and size, later to be modified, like any other part of the skeleton, by the conditions and functional demands put upon it. It remains as long

as its support is required, and then the superfluous part is gradually absorbed as the repaired bone resumes its function. The medullary canal is reestablished as absorption of the transplant progresses. The primary function of the transplant is the alignment of the fragments. Grafting of the transplant to the fragments is secondary, but very desirable.

The operative technique demands the rigorous application of the rules of asepsis as distinguished from antiseptics. Iodin preparation is prohibited. Antiseptics destroy the living bone cell of the transplant as quickly and surely as they destroy the pyogenic germ.

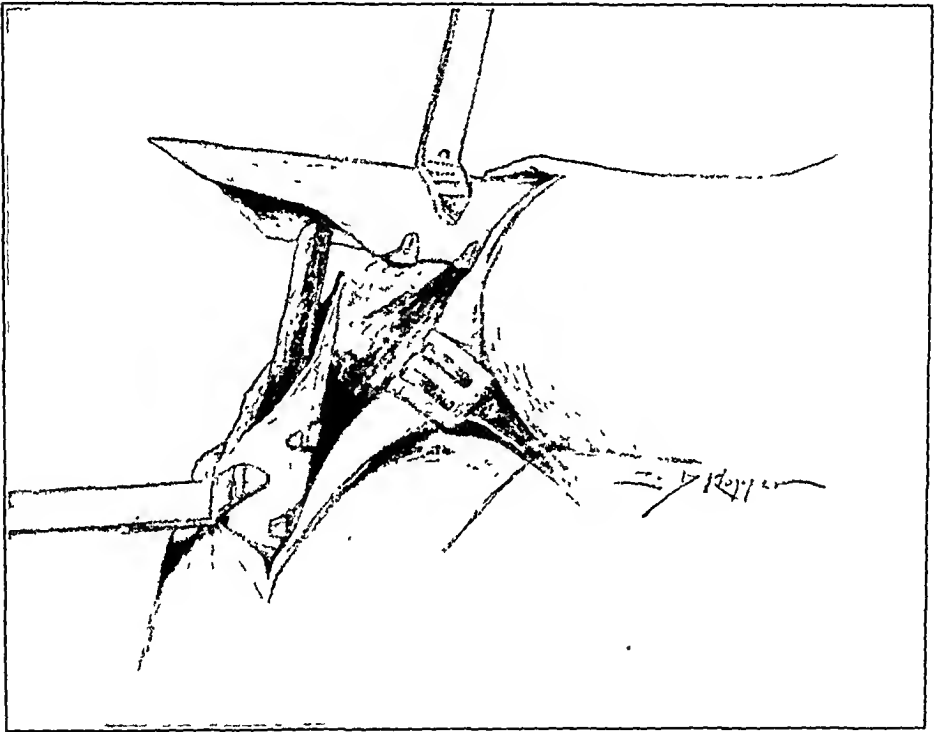


FIG. 4.—Introduction of the transplant in autoplasmic repair of spiral fracture of the tibia.

The fracture in the tibia is exposed by a flap incision, so that the repaired fracture will not be directly exposed to the danger of a skin wound. The fibula is fractured with a chisel at about the same level. The fragments of the tibia are secured by small Lowman clamps for manipulation, and are elevated. The detritus produced by the injury is cleared from the wound and the fragments are prepared for the transplant. The medullary canal of each fragment is cleared, with a bone curette, of that part of the marrow which has been disturbed by the traumatism, hemorrhage or inflammation, and then examined and measured with calipers to determine the shape and size of the transplant needed to mortise the fragments together.



A transplant is usually secured from the upper part of the crest of the same tibia. In length the transplant should be sufficient to extend into each fragment at least 2.5 cm. It is fitted to the irregularities of the upper fragment so that it will slip in and out. The other end of the transplant is fitted and driven into the lower fragment. If the transplant is too large it will split the fragment and the fixation will be destroyed. Care is exercised to make the irregular fitting between the transplant and each fragment correspond, so that when the transplant is in final position the fragments will be locked by it in correct rotation. If it is doveled or the medullary canal is reamed until it is circular the spiral fragments of the tibia will rotate and the accuracy of the reduction will be lost. The end of the transplant projecting from the lower fragment is manipulated

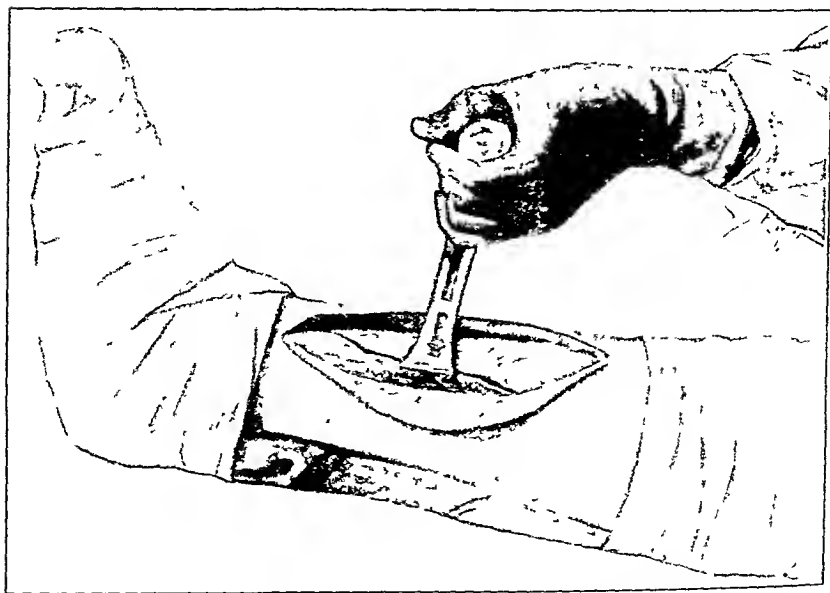


FIG. 5.—Immobilization of the fragments over the transplant, before closure of the wound and application of the cast, in spiral fracture of the tibia.

into the prepared upper fragment and the leg is straightened (Fig. 4). The muscles of the leg immediately contract and bring the fragments firmly together in alignment over the transplant. One Lowman clamp is now removed and the other is slipped over the repair so as to grasp the ends of both fragments (Fig. 5). The leg is elevated by means of the clamp and a narrow, sterile, moulded plaster splint, previously prepared and dried, is applied to the posterior part of the leg with sterile bandages above and below the wound. The clamp is removed. The wound is closed in layers by catgut sutures and dressed. A circular plaster-of-Paris cast is applied over all. The immobilization is not disturbed during the convalescence.

CASE I.—*Spiral fracture of the tibia and impacted fracture of the fibula.*

M. W., aged forty-four years, Swedish, teamster, was admitted to Cook County Hospital March 13, 1916, suffering with a broken left leg, produced by slipping and falling on the sidewalk the previous day.

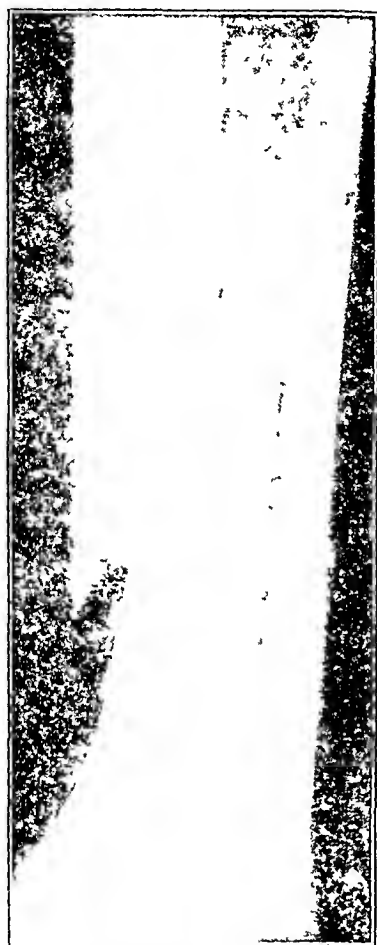


FIG. 6.—Case I. Roentgenogram of spiral fracture of the tibia.

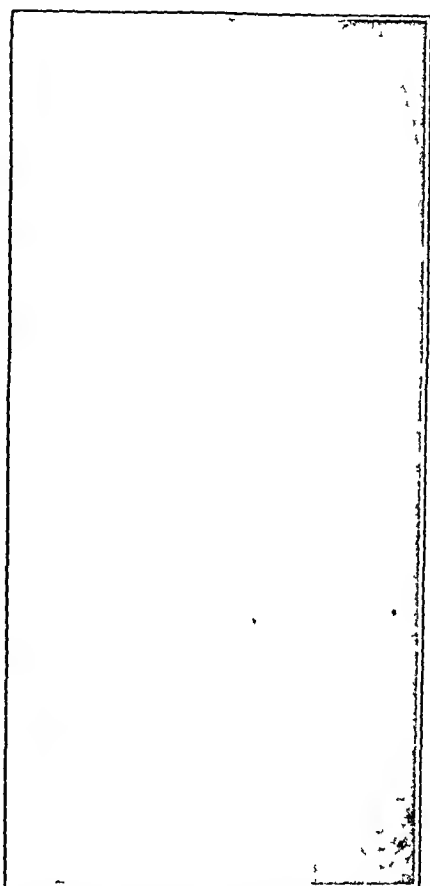


FIG. 7.—Case I. Roentgenogram of impacted, rotated fracture of the fibula, preventing reduction of the fracture in the tibia.

Roentgenograms revealed a spiral fracture of the tibia, with displacement and overriding of 2.5 cm. (Fig. 6) and an impacted, rotated fracture of the upper end of the fibula (Fig. 7).

Failing to effect reduction by external manipulation, open operation for autoplasmic repair was performed March 20, 1916. The fracture was exposed by a flap incision. It was impossible to replace the lower fragment of the tibia because of the position of the impaction of the fragments of the fibula. To facilitate reduction of the fragments of the tibia the fibula was broken at the same level.

A transplant 15 cm. in length was obtained from the crest of the same tibia well above the fracture. The thickness of the transplant was determined by caliper measurements of the medullary canal of the fragments and the defect between them. After careful fitting the transplant was driven into the medullary canal of the lower



FIG. 8.—Case I. Roentgenogram of autoplasmic repair of spiral fracture of the tibia, immediately after operation, showing the transplant across the line of fracture, securing the fragments in reduction.



FIG. 9.—Case I. Roentgenogram of autoplasmic repair of spiral fracture of the tibia, eight weeks after operation, showing the transplant grafted into the medullary canal and bony union of the fracture.

fragment. The free end of the transplant was then manipulated into the medullary canal of the upper fragment. The fragments were placed in accurate reduction, with a clamp holding them in position during subsequent manipulations. A sterile, posterior, moulded splint was bandaged to the leg above and below the wound for

temporary support. The clamp was removed, the wound closed, dressed with gauze and a circular cast applied over all.

A roentgenogram taken after the operation revealed the transplant in the medullary canal across the line of fracture of the tibia, supporting the fragments in anatomical reduction (Fig. 8).

The immobilization was not disturbed for four weeks, when healing appeared to be complete and union of the fracture was firm. A roentgenogram taken eight weeks after operation revealed good union of both bones (Fig. 9). Functional recovery was apparently complete.



FIG. 10.—Case II. Roentgenogram of compound spiral fracture of the tibia.

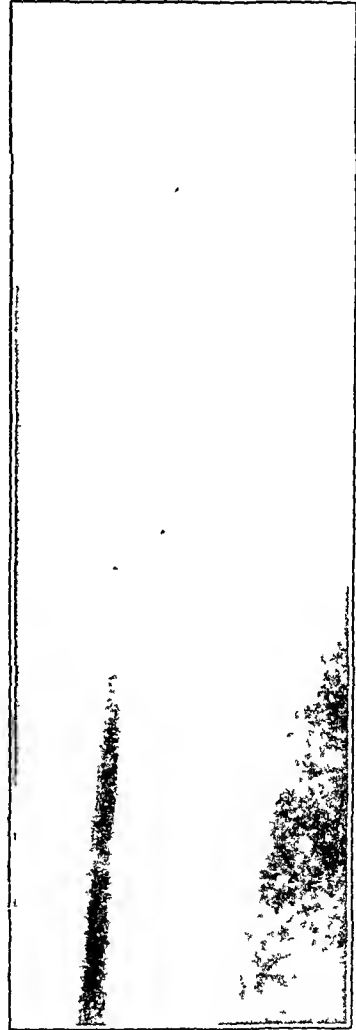


FIG. 11.—Case II. Roentgenogram of rotated spiral fracture of the fibula.

*CASE II.—Compound spiral fracture of the tibia and impacted fracture of the fibula.*

J. W., aged forty years, American, bench worker, was admitted to Cook County Hospital on May 11, 1916, with a compound

fracture of the right leg. He gave a history of having been thrown while scuffling. His toe was caught under the edge of a carpet and his leg twisted as he fell.



FIG. 12.—Case II. Roentgenogram of autoplasmic repair of spiral fracture of the tibia, five weeks after operation, showing the transplant grafted into the medullary canal across the line of fracture and bony union of the fracture.



FIG. 13.—Case III. Roentgenogram of a spiral fracture of the tibia and an impacted fracture of the fibula.

Examination showed a fracture of the tibia, with an external wound communicating with the fracture. Roentgenograms revealed a long spiral fracture of the lower third of the tibia (Fig. 10), accompanied by a rotated, impacted fracture of the fibula immediately below its head (Fig. 11). The lower fragment of the tibia was rotated and displaced outward. There were 2.5 cm. overriding of the fragments.

The wound was cleansed and dressed and the extremity was immobilized in a fracture-box. Sterile healing of the wound of the soft parts was complete in three weeks.

The position of the fragments not having been changed by treatment, open operation for reduction and fixation of the fracture by the same technic as in Case I was performed May 31, 1916.

When the cast was removed at the end of five weeks, good union of the fracture was present (Fig. 12).

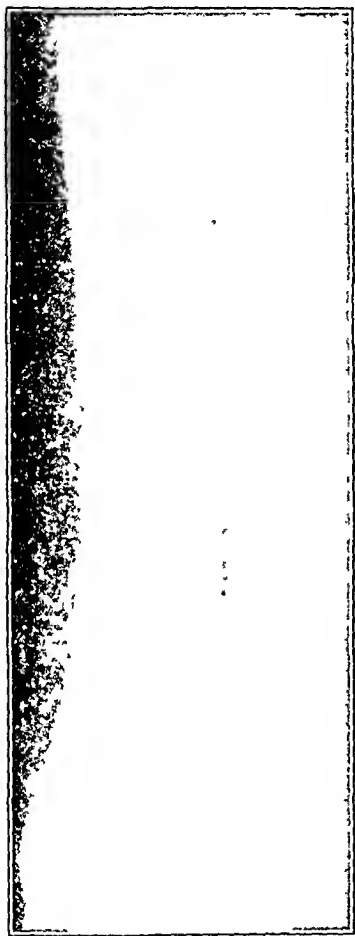


FIG. 14.—Case III. Roentgenogram of autoplasmic repair of spiral fracture of the tibia, two months after operation, showing the transplant grafted across the line of fracture and bony union of the fracture.



FIG. 15.—Case III. Roentgenogram of autoplasmic repair of spiral fracture of the tibia, eighteen months after operation.

*CASE III.—Spiral fracture of the tibia and impacted fracture of the fibula.*

L. K., aged thirty-three years, American, laborer, was admitted to Cook County Hospital January 10, 1914, with a fracture of the left leg. A roentgenogram showed a spiral fracture of the tibia and an impacted fracture of the fibula. There was overriding and complete displacement of the fragments of the tibia (Fig. 13).

After repeated failures of reduction by external manipulation

and traction, open operation for autoplasmic repair was performed two weeks after injury. The technic of the operation was similar to that used in Case I.



FIG. 16.—Case III. Roentgenogram of autoplasmic repair of spiral fracture of the tibia, eighteen months after operation, showing absorption of the greater part of the transplant and reestablishment of the medullary canal.



FIG. 17.—Case III. Roentgenogram of the same area shown in Fig. 16, thirty months after operation, showing practically no further absorption of the transplant

Firm union appeared to be present when the cast was removed four weeks after operation. A roentgenogram taken eight weeks after operation shows anatomical reduction of the fragments of the tibia and bony union of the fracture (Fig. 14). A roentgenogram taken eighteen months after operation shows complete bony repair of all fractures, but with much less callus surrounding the fractures of the tibia than those of the fibula (Fig. 15). It also shows partial

absorption of the transplant. The medullary canal has been reestablished, and apparently only that part of the transplant remains which is needed for the functional support of the tibia (Fig. 16).

A roentgenogram of the tibia taken thirty months after operation shows the condition of the transplant to be almost identical with the examination of the previous year. The absorption of the transplant has apparently ceased. What remains seems to have become a permanent support to the tibia at the point of the healed fracture, correlating the strength of the bone with its functional necessities (Fig. 17).

CONCLUSIONS. 1. Treatment of spiral fractures of the tibia by external reduction and external immobilization usually results in imperfect union of the fragments with defective function of the leg.

2. Treatment by open operation and autoplastie repair usually results in early good anatomical union of the fragments with restoration of the strength and function of the leg.

3. The autoplastie transplantation of bone in the repair of a recent spiral fracture of the tibia is a capital operation, which requires careful technic, capable assistants and aseptic surroundings.

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## ACHYLIA GASTRICA AND CHRONIC CONNECTIVE-TISSUE LIENTERY: A CLINICAL STUDY OF 322 CASES.

BY NOBLE WILEY JONES, M.D.,  
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FOR a number of years past, especially since Adolf Schmidt devised his intestinal test diet and recognized by it certain gastrogenic intestinal affections, several disturbed phenomena of digestion have been assumed to take place in chronic achylia gastrica. First, the digestion of connective tissue has been held dependent upon its contact with free hydrochloric acid in the stomach for a sufficient length of time; second, the emptying time of the stomach has been thought to be much shortened; third, the power of the stomach to disintegrate food and destroy bacteria has been considered much decreased. Reasoning *a priori* gastrogenic intestinal catarrh and dysentery have been looked for as an accompaniment of achylia gastrica due to undigested connective tissue and non-disintegrated foods in general, and when such catarrh or dysentery was found in the presence of normal stomach chemistry it was assumed that for some reason an abnormal pyloric insufficiency existed. The frequent finding of irregularities in the sequence of these factors leads one to wonder what other factors enter into the cause of the associated symptoms of constipation or dysentery. of



connective tissue or mucus in the stools, or, on the other hand, why an entire absence of all subjective symptoms may exist in individuals in whom achylia gastrica is found accidentally during a routine examination. Many of our patients have been reexamined after a period of years when they considered themselves perfectly well and had returned to meat-eating, and still the anaecidity has been found to be present. What has determined the presence of health and strength in the one case, and oftentimes a semi-invalidism in the other?

**ACHYLIA GASTRICA.** These observations are based upon the clinical study of 245 cases of achylia gastrica observed in private practice between the years 1906 and April, 1916. Into this group of cases has been placed only those to which Einhorn originally gave the name, *i. e.*, those in which there is an absence of hydrochloric acid and ferments in the gastric secretion. Therefore, all instances of anaecidity associated with pernicious or other grave anemias, stomach cancer, and wasting diseases, as advanced tuberculosis or nephritis, have not been considered. The group, however, contains all cases of chronic anaecidity, both true and spurious achylia. No attempt has been made to differentiate between the psychical and chemical types of achylia of Pawlaw by means of fractional methods of studying the entire period of gastric digestion. These patients have come to us, for the most part, because of gastro-intestinal symptoms, and our present conclusions in regard to prognosis and therapy have been influenced much by our studies of the medical aspects of abdominal ptosis and its related phenomena.

The incidence of achylia gastrica in gastro-intestinal diseases is so great that it necessitates one bearing it always in mind in general diagnosis. Many times it is diagnosed cancer of the stomach, amebic dysentery, nervous diarrhea, or a neurasthenia. Stockton found, in 1909, that his 132 cases bore a ratio to other stomach diseases examined as 1 is to 20. In 1911 a review of 600 cases of mine with abdominal symptoms afforded 47 cases of achylia, or an incidence of 1 to 12.7. It is my impression that this ratio holds approximately with the larger number of cases reviewed here. Such a frequency demands a more consistent study of the condition than has thus far been accorded it.

In reviewing my series of cases I wish to present merely some clinical features which I believe to be of importance. Especially is this so in relation to the prognostic and therapeutic aspects. Table I is a *résumé* of the salient features of the 245 cases. There are 96 males and 149 females. In both groups the largest number of cases appear during those years when there is the greatest strain put upon the mind and body of the individual, *i. e.*, between the years of forty and sixty in man, when he is bearing his greatest responsibilities, and during the active child-bearing and menopause periods in women. Viewed from a stand-point of

the body build, 132 have an asthenic type of structure and 113 possess broad frames. But as the general asthenic state is not confined to individuals of asthenic type of build, the presence of general asthenia in 182 cases is of more significance. Many times the patient dates the beginning of his symptoms to some definite exciting cause; a pregnancy, an infectious fever, an operation, or a period of some emotional stress. More and more, as the earlier cases were observed through the succeeding years and relapses studied, did this factor of an exciting cause leading to a general asthenia become apparent. Ten patients of the series stated that the beginning of their ill health dated back to definite periods of excessive worry. In the severe general asthenics many had a history of chronic gastro-intestinal symptoms from childhood on. Thus the parallelism between the onset and course of the symptoms in the majority of these patients and in a corresponding series of general asthenics with normal stomach chemistry is most striking. The presence of the general asthenic state is the one factor which stands out in bold relief from among all others.

TABLE I.—NUMBER OF CASES, 245.

Sex		Age				
		Under 15. 1 to 8 years	15 to 25. 7	25 to 40. 13	40 to 60. 59	Over 60. 16
	{ Male, 96	0	9	57	75	15
	{ Female, 149					
						Connective tissue in stools
Exciting causes	{ Leading to general asthenia . . . . .					143
	{ Absent or unrecorded . . . . .					98
Symptoms	{ Gastro-intestinal . . . . .					239
	{ Wholly referred . . . . .					43
Build	{ Asthenic type . . . . .					132
	{ Broad . . . . .					113
Associated diseases . . . . .						81
General asthenia	{ Present . . . . .					182
	{ Absent . . . . .					62
	{ Unrecorded . . . . .					1
Dysentery . . . . .						90
Constipation . . . . .						157
Mucous colitis . . . . .						35
Connective tissue in stool	{ Present . . . . .					130
	{ Absent . . . . .					66
	{ Unrecorded . . . . .					46
	{ Good . . . . .					141
End-result	{ Fair or poor . . . . .					55
	{ Unrecorded . . . . .					49

Sixty-two patients of the series gave no evidence of a general body weakness. The symptoms of this group are noticeably different from those of the asthenic group. Headaches, muscular and joint pains (so-called toxic symptoms), in addition to the gastro-intestinal distresses, usually present, were most manifest. The majority of these patients were broadly built, and there was present a gastrogenic dysentery far more frequently than in the

TABLE II

Name.	Sex.		Age.	Build.		Stomach.		Ileum.		Cecum.	Colon.	Constipation.	Dysentery.	Mucous colitis.	Stool.		Local infections.	End-result.	No. of cases.
	Male.	Female.		Broad.	Asthenic.	Position.	Emptying time, hours.	Stasis.	Regurgitation.	Mobility.	Stasis.	Prosis.			Connective tissue.	Mucus.			
W. W. B.			61			O. K.	2½	Trace	+	0	0	Trace	+	+	+	+	Fair		1
E. E. R.			60			O. K.	3½	0	+	0	0	0	0	0	+	+	Good		2
J. A. R.			39			Low	5 to 6	0	+	0	0	0	0	0	+	+	Questionable		3
Sam.			70			Low	7	0	+	0	0	0	0	0	+	+	Poor; chronic gall-bladder		4
C. W. M. T.			46			O. K.	4½	0	+	0	0	+	+	+	0	0	Good		5
A. M. T.			47			Low	0	0	+	0	0	+	+	+	0	0	Fair; psych-asthenic		6
G. T.			32			O. K.	2½	0	+	0	0	+	+	+	0	0	Good		7
C. S.			26			Low	5	0	+	0	0	0	0	0	+	+	Poor; not controlled		8
C. M. H.			56			O. K.	5½	0	+	0	0	+	+	+	+	+	Good		9
D. C. H.			50			O. K.	6	0	+	0	0	+	+	+	+	+	Good		10
R. C. H.			49			O. K.	3½	0	+	0	0	+	+	+	+	+	Good		11
I. C. B.			32			Low	3	0	+	0	0	+	+	+	+	+	Good		12
E. H.			50			Low	6	0	+	0	0	+	+	+	+	+	Good		13
E. H.			58			Low	5½	0	+	0	0	+	+	+	+	+	Fair; gall-bladder (protop.)		14
C. W. H.			48			Low	0	0	+	0	0	+	+	+	+	+	Good		15
G. L.			82			Low	0	0	+	0	0	+	+	+	+	+	Good		16
T. R. W. P.			66			Low	0	0	+	0	0	+	+	+	+	+	Good		17
A. E. W. P.			56			O. K.	4½	0	+	0	0	+	+	+	+	+	Fair; business worry		18
G. E. M.			38			O. K.	0	0	+	0	0	+	+	+	+	+	Good		19
L. V. W.			30			Low	4	0	+	0	0	+	+	+	+	+	Good		20
C. W.			35			Low	6	0	+	0	0	+	+	+	+	+	Fair; organic heart disease; died later		21
W. E. W.			36			Low	6	0	+	0	0	+	+	+	+	+	Poor; chronic gall-bladder; died from operation		22
E. P. T.			53			Low	5	+	+	0	+	+	+	+	+	+	Good; chronic arthritis		23
I. S.			63			O. K.	5	0	+	0	+	+	+	+	+	+	Fair; cardio-vascular		24
Las.			57			Low	0	0	+	0	+	+	+	+	+	+	Good		25
R. L. M.			47			Low	5½	0	+	0	+	+	+	+	+	+	Questionable		26
L. B. N.			26			Low	3½	0	+	0	+	+	+	+	+	+	Poor; psychoneurosis		27
G. S.			58			O. K.	3½	0	+	0	+	+	+	+	+	+	Good; arrested tuberculosis		28
Totals	7	21		0	19	O.K. 11 Low 17		9	3	11	7	17	18	20	5	2	14	17	10

asthenic group. These patients also did not lose weight or strength; and, what is of great significance, they received, for the most part, quick relief from their symptoms as soon as the bowel condition was corrected. This was in sharp contradistinction to the asthenic type.

An attempt was made in the study of 28 cases of achylia to harmonize, if possible, the occurrence of connective tissue in the stool and the presence of dysentery or constipation with an early emptying time of the stomach, and with the presence of abdominal ptoses and local stases. The details of this study are to be found in Table II and a *résumé* of the data in Table III. Certain deductions may be made even from this limited number of observations.

TABLE III.—ACHYLIA GASTRICA. RÉSUMÉ OF 28 CASES.

Build	{	Asthenic type . . . . .	19	
		Broad type . . . . .	9	
Position of stomach	{	Low . . . . .	17	
		Normal . . . . .	11	
.				
				Connective tissue in stools.
Less than 4 hours,	2 {	Constipation . . . . .	0	—
		Normal . . . . .	1	0
		Dysentery . . . . .	1	1
Four hours or over,	15 {	Constipation . . . . .	13	9
		Normal . . . . .	1	1
		Dysentery . . . . .	1	0
.				
Less than 4 hours,	5 {	Constipation . . . . .	1	1
		Normal . . . . .	1	1
		Dysentery . . . . .	3	3
Four hours or over,	6 {	Constipation . . . . .	6	3
		Normal . . . . .	0	—
		Dysentery . . . . .	0	—

The majority of instances of constipation were associated with an emptying time on the part of the stomach of four or more hours, and the majority of them are found also in ptotic individuals in whom the mechanical factors of constipation, as regards position, play a part. Of the 5 cases of chronic dysentery, 4 of them were associated with a too rapid emptying of the stomach, and 3 of these were found in broadly built individuals in whom the stomach occupied a relatively high position in the abdomen. There was found no guiding relationship between ileum stasis, cecum mobile, or cecum stasis, general colon stasis and ptosis, and the presence of connective tissue, or the quantity of mucus in the stool, or with the occurrence of constipation or dysentery, or, again, with the emptying time of the stomach. The size, position, and activity of the stomach showed no distinguishing features in the achylia cases from other individuals. In the majority of the asthenically built patients the stomach was low, atonic, and the peristaltic waves feeble. The organ also did not empty itself of the greater part of

the meal rapidly and then lie dormant with a moderate rest for a longer time, as one might assume. The stomach picture under the screen appeared tonic or atonic, depending upon the degree of general asthenia, absent or present, in the individual. It was wholly impossible to distinguish the atonic stomach of an asthenic achylic patient from that of the ordinary asthenic patient with normal stomach chemistry. Focal infections involving mostly the teeth and the tonsils were met with in variable degree ten times. No causative relationship could be ascribed to them.

CHRONIC CONNECTIVE-TISSUE LIENTERY.<sup>1</sup> The failure on the part of the stomach in the presence of normal chemistry to digest connective tissue, and the latter's appearance in abnormal quantities in the stool, frequently gives rise to much the same series of gastro-intestinal disturbances that are seen in chronic achylia. The symptoms seem also to bear the same relation to the exciting causes of general asthenia. The type of build of the patient in whom the condition is met likewise influences the response to treatment in the same way, for in the ptotic type of individual the added factor of general asthenia is usually encountered, and this must be overcome before the patient becomes symptom-free.

It has been assumed, as stated above, that the emptying time of the stomach determined the presence or absence of undigested connective tissue in the stool. So far as I know no accurate observations have ever been made to determine this point. There are met in routine röntgenological examinations of gastro-intestinal cases many instances of gastric hypermotility due, for instance, to duodenal ulcer or periduodenal lesions, but I have been often impressed with the fact that these patients do not frequently have connective tissue in their stools from intestinal test diets. In the hopes of obtaining some guiding data in this group of cases I have reviewed 77 cases observed from 1906 to April, 1916. The resulting general data is set forth in Table IV, and 10 of these cases have been studied more in detail, as itemized in Table V. In the latter table the stomach's emptying time of Cases No. 1 and No. 3 cannot be considered, as the time was not accurately observed; but in the remaining 8 cases 6 were of a broad non-ptotic type of build, and it is to be noted that in 5 of these 6 cases the stomachs were emptied in two and one-half, two and one-half, three, two, and two and one-half hours respectively. Again, the remaining 2 patients (No. 4 and No. 10) were of the asthenic type of build with prolapsed stomachs, and the emptying time was six hours and seven plus hours respectively. In other words, the mechanical influence of position, coupled with a lack of muscular tone, brought about this difference in motility, although each patient possessed three plus connective tissue in his stools. Chronic dysentery is more

<sup>1</sup> Chronic connective-tissue lienterly is here arbitrarily defined as the presence of abnormal quantities of undigested connective tissue in the stool without regard to the derivation of the word lienterly.

frequent in patients of a broad type of build, and obstinate constipation is much more frequent in those with abdominal ptosis. The reasons why a hypermotility of the stomach existed in many cases, why connective tissue was found in the stools of constipated patients possessing either a hypermotility or a delayed motility, or why chronic dysentery is associated in one case with a hypermotility of the stomach and in a second case with a delayed motility are not known. They concern the physiological factors of gastric and colon motility, which are as yet not understood.

TABLE IV.—CHRONIC CONNECTIVE-TISSUE LIENTERY. 77 CASES.

		Age						
		Under 20.	20 to 30.	30 to 40.	40 to 50.	50 to 60.	Over 60.	
Sex	Male, 34	1	5	11	11	4	2	
	Female, 43	1	10	18	5	4	5	
Type of build	Broad, 42	Regular	.	.	.	.	.	10
		Constipation	.	.	.	.	.	16
		Dysentery	.	.	.	.	.	10
		Alternating	.	.	.	.	.	6
	Asthenic, 35	Regular	.	.	.	.	.	3
		Constipation	.	.	.	.	.	20
		Dysentery	.	.	.	.	.	3
		Alternating	.	.	.	.	.	9
Mucous colitis		.	.	.	.	.	.	13
Focal infections		.	.	.	.	.	.	15
		Good.	Fair.	Poor.	Unknown.	Died.		
End-results		47	7	5	17	1		

**PROGNOSIS.** It has seemed to me that theoretically all cases of uncomplicated chronic achylia gastrica and chronic connective-tissue lienteria were amenable to treatment. Practically this end is not always attainable, (1) because of lack of sufficient control over the individual, and (2) because of one's inability to always remove the exciting cause of an accompanying general asthenia. Especially is this true when an emotional stress, as worry, cannot be overcome.

The prognosis of either condition in a physically strong individual is always good. The so-called toxic symptoms and the gastrointestinal distresses disappear, as a rule, quickly as soon as the diet is corrected and the frequently accompanying colitis is allayed. In the asthenic type of patient, however, the problem is different. The added factor of general asthenia demands oftentimes the long detailed course of body rebuilding which is necessary to successfully treat the general asthenic patient that possesses a normal stomach chemistry. The asthenic achylic patient is oftentimes a difficult patient to handle. A large percentage of them must be treated in hospital under control if a satisfactory end-result is to be obtained. In place of viewing the achylic patient in a semihopeless manner, as is still customary, we have learned to expect good results when the

TABLE V

Name.	Sex.		Age.	Build.		Stomach.		Ileum.		Cecum.	Colon.	Constipation.	Dysentery.	Mucous colitis.	Stool.		Local infections.	End-result.	No. of cases.
	Male.	Female.		Broad.	Asthenic.	Position.	Emptying time, hours.	Stasis.	Regurgitation.	Mobility.	Stasis.	Ptois.	Stasis.		Connective tissue.	Mucus.			
E. M. O'B.	1	:	42	+	:	O. K.	6	0	0	0	0	0	0	0	+	+	+	Cardiovascular impairment	1
E. B. L.	1	:	43	+	:	O. K.	2½	0	0	0	0	0	0	0	+	0	0	Good	2
H. A. Mc.	1	:	32	+	:	O. K.	6	0	0	0	0	0	0	0	+	0	0	Good	3
H. R. S.	1	:	28	+	:	O. K.	6	0	0	0	0	0	0	0	+	0	0	Good	4
I. P.	1	:	49	+	:	O. K.	2½	0	+	0	0	0	0	0	+	0	0	Good	5
K. L.	1	:	31	+	:	O. K.	6	0	+	0	0	0	0	0	+	0	0	Fair	6
C. M. R.	1	:	45	+	:	O. K.	6	0	+	0	0	0	0	0	+	0	0	Poor; goitre; O. H. D.; chronic arthritis	7
H. W. C.	:	1	67	+	:	O. K.	2½	0	0	0	0	0	0	0	+	+	0	Good	8
H. H.	:	1	35	+	:	O. K.	7+	0	0	0	0	0	0	0	+	+	0	Good; psychoneurosis	9
L. B. D.	:	1	29	:	+	Low	7+	0	0	+	0	+	0	0	+	+	0	Good	10
Totals	5	5		8	2	O. K. 9 Low 1		2	1	1		2	2		10	7	3		

patient's adherence to these principles can be maintained over a sufficient length of time.

**TREATMENT.** The principles of treating achylia gastrica and connective-tissue lientery embrace in all cases two factors: (1) the avoidance of connective tissue during at least the symptom-bearing period, and (2) the *mechanical preparation* of all food for entrance to the small intestine. Sufficient chymification of food rarely takes place in the anacid stomach whether it remains a short or a long period of time. The thorough preliminary cooking of vegetables is necessary in order to separate masses of vegetable cells. The more thorough the mechanical division of the food is carried out by cooking, sieving and chewing it, the quicker is the secondary bowel disturbance relieved. With the general asthenic type of patient the accompanying general asthenia must be definitely overcome before relief can be expected. The fundamental principles of overcoming the general asthenic state apply here as elsewhere. The use of hydrochloric acid theoretically to replace the acid reflex of Pawlaw is, from a practical stand-point, an individual matter. Many patients are symptomatically relieved by its use while others experience increased sourness and stomach irritation. Its use must be governed accordingly.

After the patient has regained his normal health he may, as a rule, return to meat-eating with impunity; at least, many do and apparently without harm. Why this is so it is impossible to say. Schutz and others have thought best to explain the production of the resulting gastrogenic intestinal state by reason of the long-continued failure of the acid reflex bringing about eventually an insufficiency of intestinal digestion, more especially that of the pancreas. Changes in the flora and the biochemistry of the bowel result. Against this view, it seems to me, would be the fact that insufficient starch and nuclein digestion rarely is found in the stools of chronic achylics. The question of restoring a normal fund of general body tone has seemed to me to be the deciding factor in many of these cases. The bowel then simply is capable of throwing off irritating foods without receiving harm from them. As soon as the general body strength is lowered the power of the bowel to do this is reduced and symptoms appear. This explanation does not seem to hold true in some of the broadly built patients who suffer symptoms without loss of body strength. Some patients of this type are never able to return to meat-eating without ill effects.

**CONCLUSIONS.** 1. Achylia gastrica is usually associated with a too rapidly emptying stomach in the broadly built, non-ptotic person. In the ptotic individual the factors of position and atonia seemingly tend to overbalance this tendency, and the emptying time of the stomach may be as long as seven hours or longer.

2. Both of the above conclusions seemingly hold true in the case of chronic connective-tissue lientery.



3. In both groups of cases dysentery is prone to occur in the non-ptotic type of person in whom a hypermotility of the stomach is present. Contrariwise, constipation is apt to be found in the ptotic individual in whom the mechanical factors leading to constipation exist.

4. The symptoms and response to treatment in both groups of cases differ noticeably according to the presence or absence of the general asthenic state.

5. Both groups of cases are distinctly amenable to treatment, and good end-results can be obtained under suitable conditions.

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### DIGITALIS AND THE CONTROL OF AURICULAR FIBRILLATION AND AURICULAR FLUTTER, WITH ELECTROCARDIOGRAMS ILLUSTRATING THE EFFECT.

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THE intention of these remarks is to offer for discussion and in that way emphasize a method of using digitalis in some forms of cardiac decompensation and arrhythmia.

No review of the physiological action and preparations of digitalis will be attempted, but it is necessary to state the preparation, the size of the doses, and the method of administration that the indications which guided in their use may be understood. To illustrate the type of case and the desirable and expected action of digitalis, 4 cases will be briefly related and the electrocardiograms showing various effects exhibited.

In the choice of preparations, preference has been given in the order related to the tincture, the infusion, digipuratum, and, for emergencies, crystalline strophanthin (Thoms), or methyl-gouabain, which Hatcher believes to have the same action. The tincture was given in 15 to 30 minims, not drop doses, every four hours, as a maximum dose. The infusion in  $\frac{1}{2}$ -ounce doses was used when edema was extreme. If objection was made by the patient to the fluid preparations, digipuratum was given in minimum doses of four tablets in the twenty-four hours. If none of these preparations could be used, or immediate action was desired, crystalline strophanthin (Thoms), 0.0005 gram, diluted in 2 to 4 c.c. of freshly distilled water, or salt solution (this is the equivalent of 1 to 4000 to 1 to 8000), and injected slowly into a vein, or half this dose may be given twice a day. Strophanthin in such a dose

should not be given if the patient has had any of the digitalis bodies during the previous week, nor should it be repeated within twenty-four hours. These precautions must be observed, since digitalis and strophanthin are synergists, and in the circumstances stated the total effect of absorbed digitalis and of the rapidly absorbed strophanthin might very well be quickly and fatally toxic. The amorphous preparations of strophanthin are only about half the strength of the crystalline, and unreliable.

Nausea and vomiting may be produced by digitalis, and they are also distressing complications of heart failure. If these symptoms have resulted from the digitalis, it has required three or four days of dosage with the drug; but if they belong to the heart failure, it follows immediately from any distasteful potion. The element of time of onset of the nausea and vomiting is important in the differential. When nausea or vomiting is present, precluding the use of the drug by mouth, and the digitalis effect is desired, strophanthin may be used intravenously, or an enema may be given, consisting of 120 c.c. of milk containing either 2 c.c. of the tincture or 30 c.c. of the infusion of digitalis. If the digitalis produces nausea before it slows the heart it will avail nothing to change the preparation, in the belief that by so doing the nausea will cease, for the nausea is the result of the digitalis acting on the vomiting center in the medulla. Eggleston and Hatcher<sup>1</sup> believe they have shown conclusively by animal experiment that both vomiting and diarrhea are of central origin. Nausea occurs most frequently before slowing of the heart in patients with marked arteriosclerosis.

In arteriosclerotics with fibrillation of the auricle and Cheyne-Stokes type of periodic breathing, digitalis may prolong the period of apnea and exaggerate the dyspnea portion of the cycle. Small doses, 5 minims of the tincture of belladonna, may give prompt relief and should be continued until digitalis effect is relieved.

Working with isolated coronary arteries, C. Voegtlin and D. I. Macht<sup>2</sup> believe they have shown that digitonin causes a relaxation of the arterial wall, while digitoxin and digitalin cause constriction. The great efficacy of the infusion is due probably to the digitonin promoting the circulation and nutrition of the heart muscle. The persistence of the action of digitalis will vary, depending upon the amount absorbed and fixed in the tissues, which amount depends upon the elimination being less than the absorption.<sup>3</sup>

Some cases after full doses of digitalis may require ten to fourteen days before all evidence of the digitalis effect disappears. There need be no fear of cumulative effect of digitalis when given by the mouth in doses to control fibrillation.

<sup>1</sup> Jour. Pharm. and Exper. Therap., 1912, iv, 113, and Jour. Am. Med. Assn., 1913, ix, 499.

<sup>2</sup> Jour. Pharm. and Exper. Therap., 1913, v, 1.

<sup>3</sup> Hatcher, R. A.: Arch. Int. Med., 1912, x. Eggleston, C.: Jour. Am. Med. Assn., 1912, lix, 1352.

The first case demonstrates how promptly strophanthin intravenously can reduce the ventricular rate in fibrillation of the auricle, and how that rate subsequently can be controlled by digitalis.

CASE I.—M. Q., aged thirty-two years, married, admitted complaining of palpitation, shortness of breath, vomiting, and swollen legs. Her family history is irrelevant. As a child she had measles, chicken-pox, typhoid, and at fifteen her first attack of rheumatism. She had three children and no miscarriages, and seven months before admission her last child was born. Six months before admission she had pneumonia, since which time she has been short of breath on exertion. Five days before admission her feet swelled, the amount of urine diminished, and her heart began to palpitate. On examination she was cyanotic, orthopneic, gasping for breath, with paroxysms of coughing and at times vomiting; her legs were greatly swollen and her back up to the dorsal region was edematous; the pulsating liver was enlarged to the level of the umbilicus and the lungs had coarse and fine rales up to the level of the angles of the scapula. The apex of the heart was felt in the sixth space 13 cm. to the left of the midline, and the action was grossly irregular and tumultuous, with ventricle contracting at the rate of 135 to 150 per minute (Fig. 1); the count at the wrist was only 80 per minute, a deficit of 50 to 70 per minute. Ten hours after admission an intravenous injection of crystalline strophanthin, 0.5 mg. was given. Half an hour later she was breathing quietly and could lie on three pillows with comfort. Digipuratum, four tablets per day for five days, were given until the ventricular rate decreased to 85 per minute. Four days later, as the rate of the ventricle increased, she was given  $\frac{1}{2}$  ounce of the infusion twice a day. While taking this amount of the infusion the edema diminished, the urine increased in quantity, and the heart frequency was controlled. She regained her strength and left the hospital. To control (Fig. 2) the heart rate, however, it has required the continued use of a maximum daily dose of three-quarters of an ounce of the infusion of digitalis. With this dose she is able to be about the house doing light tasks, but diminishing or discontinuance of the dose means immediate distress and disability. The need of continuing for the remainder of life such a dose of digitalis as will control the heart rate must be emphasized, for in cases with fibrillating auricles this point is very often neglected, and after a short interval without digitalis these cases return in great distress. The neglect to prescribe or use digitalis in this manner occurs not only in hospital and dispensary but also in private practice, and the withholding seems to be due to ignorance of the necessity for the continued action of the digitalis. Each case must be tried out to discover the amount of the particular preparation of digitalis which will be required to control the heart action. Not only does

the strength of the preparations of the tincture or infusion made by different firms vary, but it must always be borne in mind that each individual reacts in a different degree to the same preparation,



FIG. 1.—Case I. M. Q., taken June 16, 1914, before strophanthin was given, shows auricular fibrillation, with a ventricular rate of 140 to 150 and a positive or upward directed *T*-wave in lead II.

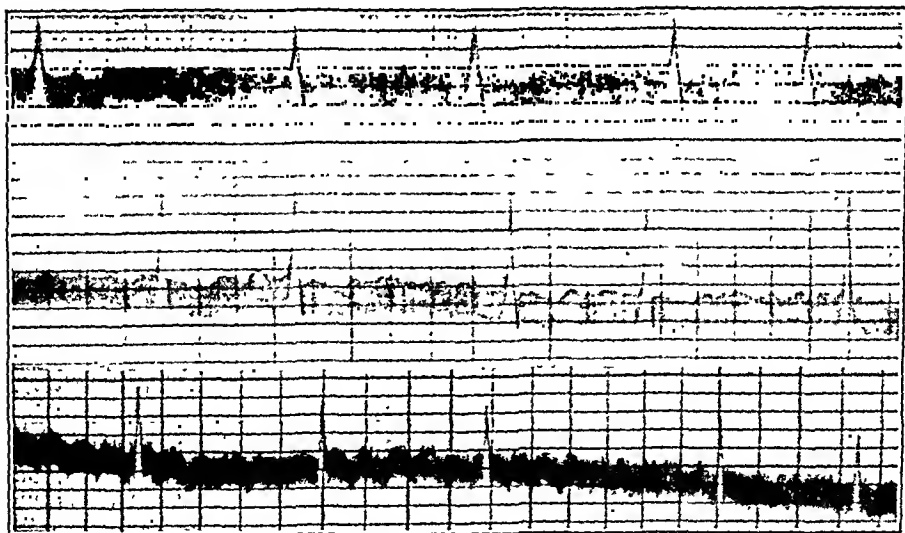


FIG. 2.—Case I. M. Q., taken November 19, 1914, shows the slower rate of the ventricle to be 80 to 90, though the auricle continues to fibrillate. The slower rate is maintained by digitalis, the second effect of which is shown by the negative or downward-directed *T*-waves of lead II.

and therefore it follows that the two variables of patients and preparations must be tried out.

The regulation of the ventricular rate is brought about by the action of digitalis on the mechanism conducting the impulses to contract over the auriculoventricular muscle bridge or bundle of

His. Two demonstrated facts show that a great part, if not all, of its inhibiting effect is due to stimulation of the vagus nerve endings in the auriculoventricular bundle: (1) pressure<sup>4</sup> on the vagus in the neck can slow the rate of the ventricle, and (2) atropin can release the ventricle from the digitalis effect and permit the ventricular frequency to increase. When the heart muscle is only moderately damaged the increase from atropin may be as much as two or three times the slow rate, while in arteriosclerosis of marked degree the atropin may produce little or no effect unless huge (0.1 grain) doses are used. Digitalis produces or increases the functional heart block. From experimental work on the lower animals<sup>5</sup> there is evidence to point toward disturbances of the functions of contractility and conduction of the heart muscle as the cause of fibrillation, by which term is understood that condition of the auricular muscle in which the separate muscle fibers contract individually and not with coördination; the auricle remains in diastole while its walls quiver with the fibrillating muscle fibers. The numerous and rapid contractions of the auricular muscle send rapidly recurring impulses to the auriculoventricular bundle, by which they are transmitted to the ventricle, and digitalis reduces the rate at which these impulses are conducted and delivered to the ventricle; but judging from the electrocardiograms it has little or no effect on the fibrillation rate of the auricular muscle. On the rate of normally rhythmic heart, little or no effect is produced by therapeutic doses of digitalis; but in the condition of fibrillating auricle, digitalis usually produces a very prompt and profound effect. So certain and dependable is this reaction of the inhibitory mechanism of the heart to digitalis that its absence in cases of fibrillation should be interpreted as insufficient dose, inactive preparation, or extensive muscle damage. It is one method of physiologically testing the sample of digitalis.

The second case is one of fibrillation, which under a brief treatment by digitalis returned to normal sequential rhythm.

CASE II.—R. M., aged fourteen years, had measles and many attacks of tonsillitis. For two years she had heart trouble, but came to hospital for an attack of only seven weeks' duration following "catching cold." Examination showed a girl with marked orthopnea, cyanosis, and vomiting at intervals; heart very much enlarged, with the apex in the left axilla sixth space, and consolidation of the left lower lobe; a pericardial friction rub could be heard over the precordium, and in the back the interesting phenomenon was noted that the friction sound could be heard through the consolidated lung; the liver was palpable 4 cm. below the free border of the ribs. The fibrillation of the auricle was revealed by

<sup>4</sup> Robinson, G. C., and Draper, G. J.: *Exper. Med.*, 1911, xiv, 217.

<sup>5</sup> Mines, G. R.: *Jour. Physiol.*, 1914, xlv, 349. Levy, A. G.: *Jour. Physiol.*, 1914, xlix, 54.

the gross irregularity of the heart rhythm and (Fig. 3) taken March 29, 1915. She was given a small amount of morphin to make her comfortable, as she was suffering considerable pain from the pericarditis, and next day strophanthin,  $\frac{1}{5}$  grain twice a day

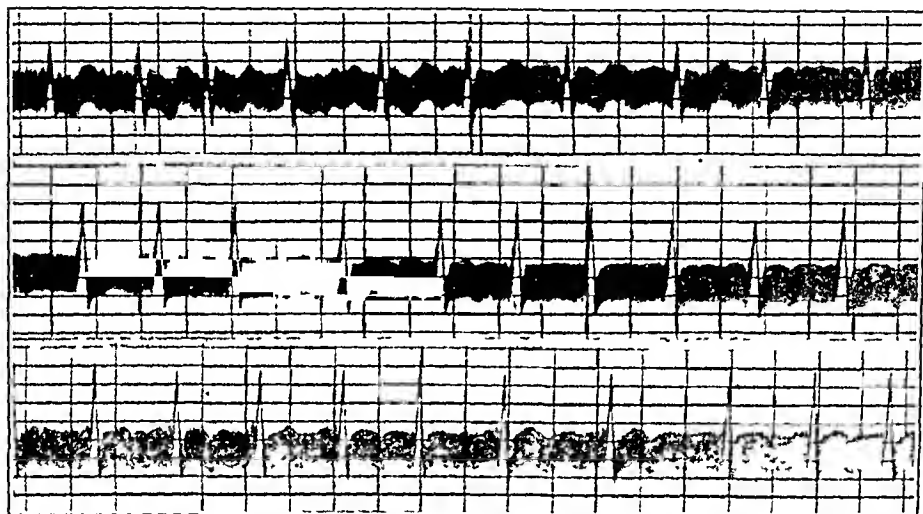


FIG. 3.—Case II. R. M., taken March 29, 1915, before digitalis effect obtained, shows the auricle fibrillating with a ventricular frequency of 157 to 170 and the *T*-waves of lead II upward or positive in direction.

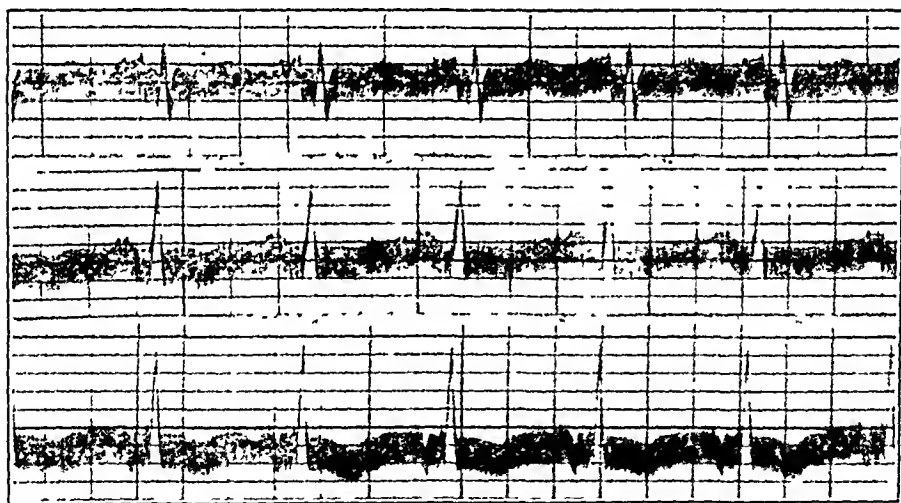


FIG. 4.—Case II. R. M., taken April 2, 1915, after digitalis was given, shows the auricle and ventricle contracting in normal or sequential rhythm at the rate of 100 and the *T*-wave of lead II is frankly negative or downward.

hypodermically. On the fourth day, because of nausea, she was given tincture of digitalis, 30 minims in milk (120 c.c.) as a rectal enema and repeated every four hours. After eight doses the ventricular rate slowed to 100 per minute and the rhythm suddenly became regular and sequential, as shown by Fig. 4, and the digi-

talis was discontinued. By sequential rhythm is understood the coördinate contraction of the auricles, followed after a definite period by the contraction of the ventricle. Once the auricle has begun to fibrillate it most commonly continues to fibrillate for the remainder of life. Rarely one may see attacks of paroxysmal tachycardia which prove to be either fibrillation or flutter and the normal rhythm be undisturbed after the attacks.

The third case is one of auricular flutter, which was altered to fibrillation by strophanthin and controlled by digitalis.

CASE III.—L. M., aged forty-two years, married, referred to me by Dr. L. Kast. As business manager of a successful London theater he was for many years under great responsibility, and it was while traveling for professional purposes in this country that he came under observation. He had always used alcohol more or less frequently in excessive amounts, and he began to smoke tobacco at fourteen. In other respects he enjoyed excellent health and denies having had venereal disease. When sixteen years of age he had his first attack of acceleration and palpitation of the heart, accompanied by shortness of breath. The first attack and others were ushered in and terminated by a sudden "thump" of the heart. The attacks frequently followed the eating of a large meal, and then would be relieved by vomiting. When the attacks occurred at other times he thought they were terminated by such procedures as holding his breath, belching, a drink of brandy, or formalypsol, very hot poultices applied to the chest, or in several instances by the jarring of a taxicab over a rough pavement. Frequently the attacks would cease during sleep. One week before he was first seen, and compelling him to terminate a hard business trip, the attack of which we have the records, began with palpitation so vigorous as to shake him visibly; the least exertion brought on great distress in breathing, and there was pain and tenderness to pressure in the epigastrium and right hypochondrium. Examination showed a man, moderately cyanotic, sitting in bed breathing quietly but frequently; the body shaken by the vigor of the heart beat. There was very slight dulness and numerous fine rales over the bases of both lungs behind. The liver was tender to pressure and the edge could be felt at a point 5 or 6 cm. below the free border of the ribs. There was no edema of the legs or ankles. The ventricular frequency was about 175 per minute and regular; the electrocardiogram (Fig. 5), showed auricular flutter, with two to one heart block. Four days later, because increasing dyspnea, pulmonary edema, cyanosis, epigastric pain, and edema of the ankles indicated an increasing heart failure, an intravenous injection of  $\frac{1}{75}$  grain of crystalline strophanthin was given. Within an hour following this dose the mechanism of the heart changed to fibrillation, record No. 386 (Fig. 6), with the ventricular rate of 115 to 130. Six days later, and before digitalis by mouth became effec-

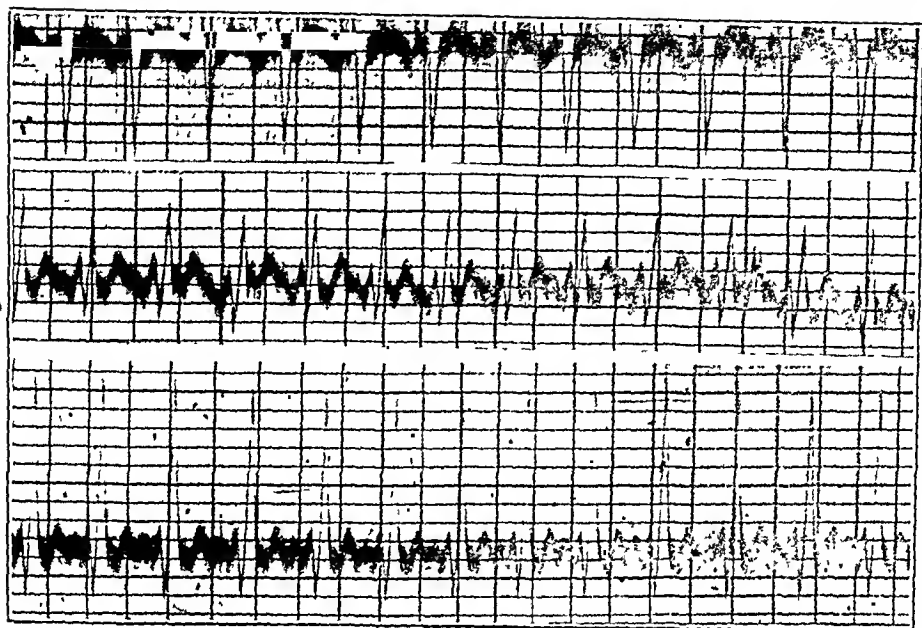


FIG. 5.—Case III. L. M., taken April 10, 1914, before digitalis was given, shows the rapid contracting auricle and ventricle of "flutter" at 175 per minute.

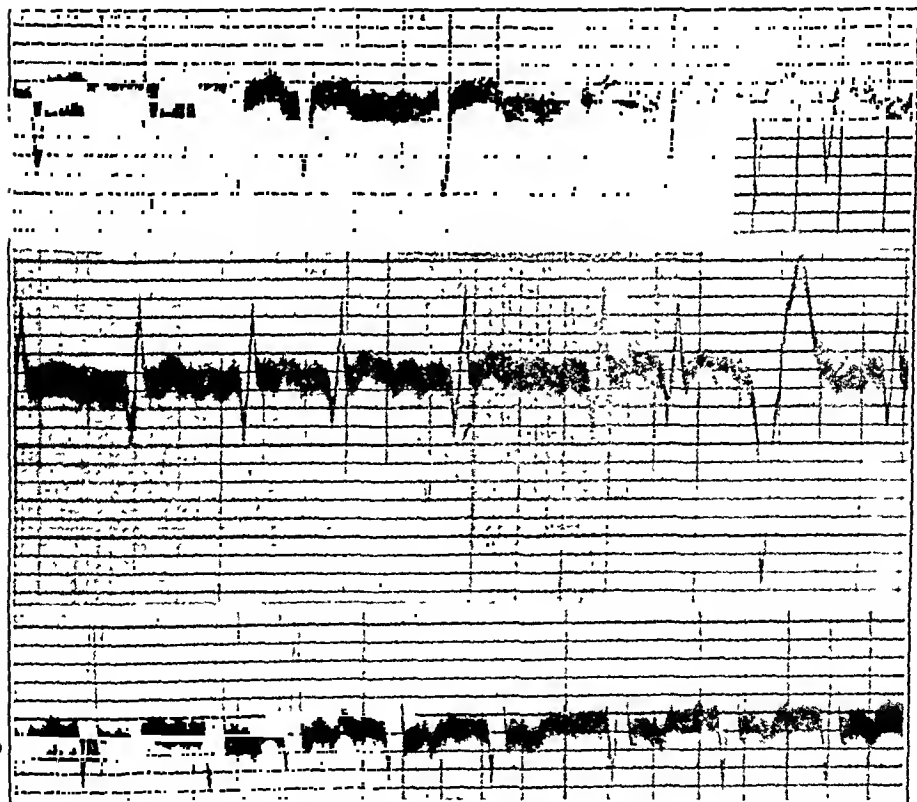


FIG. 6.—Case III. L. M., taken April 14, 1914, after strophanthin had been given and auricular fibrillation produced with a rate of approximately 115. The T-wave lead II in upward negative.



tive, the ventricular rate increased to 155 to 172, though the fibrillation persisted (Fig. 7). Under digipuratum the heart rate gradually

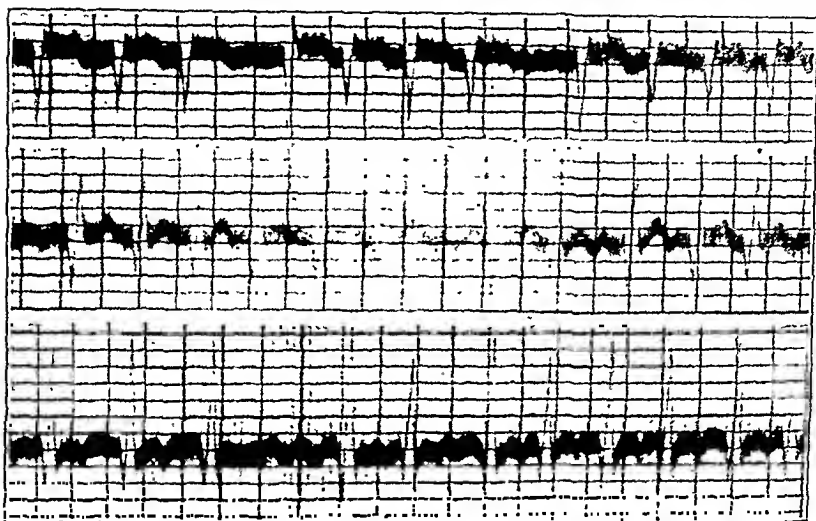


FIG. 7.—Case III. L. M., taken April 17, 1914, before the digitalis given by mouth had become effective, the ventricular rate increased to 155 to 172 per minute, but the auricular fibrillation persisted.

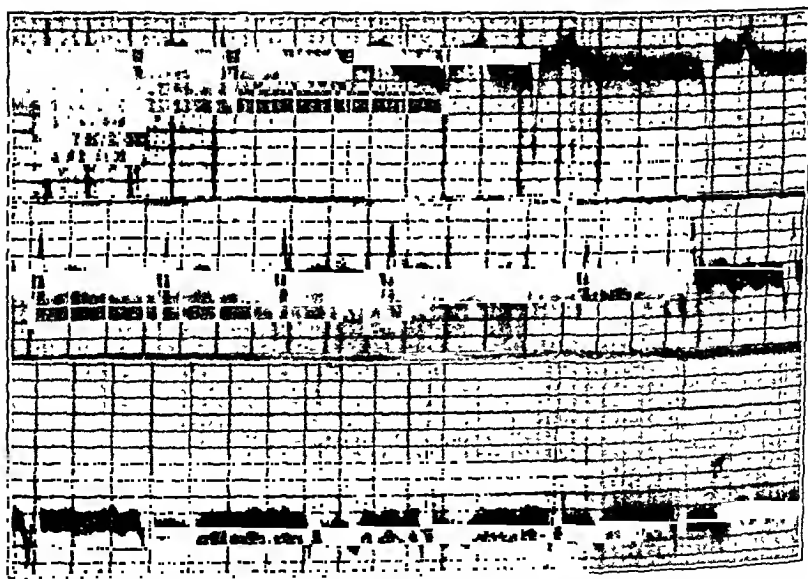


FIG. 8.—Case III. L. M., taken April 24, 1915, after the digitalis became effective, shows the ventricular rate to be about 85 per minute, with fibrillation present.

came down to 85, where it was maintained, though the fibrillation remained (Fig. 8).

CASE IV.—O. C., aged sixty-five years, was seen for the first time nine days after the removal of his prostate by Dr. J. Bentley Squier. Four days previously his heart had become very rapid and digalen in 10-minim doses, three times a day, had failed to produce any effect on the rate or rhythm. He was short of breath, restless, and conscious of the rapidly and energetically beating heart. He had the pallor peculiar to the arteriosclerotic, chronic nephritic prostatie. The blood examination showed 5,136,000 red cells; 6800 leukocytes; 55 per cent. hemoglobin. The phthalein test showed an output of 60 c.c. of urine in two hours, containing 49 per cent. of the drug.

There was an indeterminate history of rheumatism at thirty-five years of age, but otherwise his history was negative. Before operation the pulse was 88, and subsequently it was 96 to 100 until the high rate noticed on the fifth day.

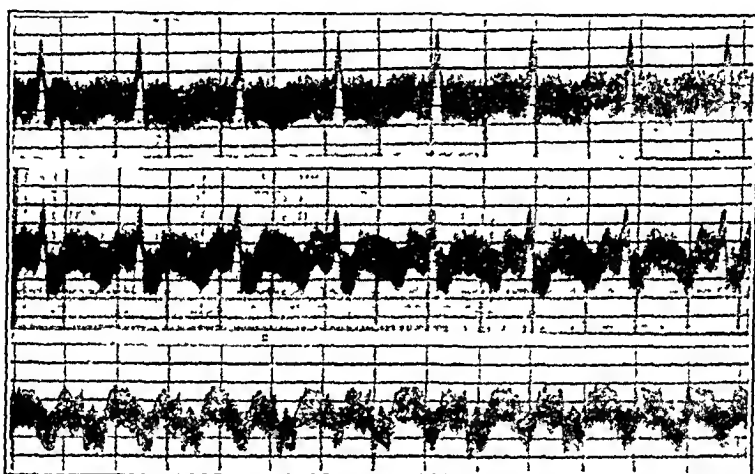


FIG. 9.—Case IV. O. C., taken February 18, 1916, shows auricular flutter at 320 per minute, two to one heart block and ventricle at 160 per minute.

The apex was in the fifth space 10 cm. to the left of the midline. The ventricular rate was about 160 per minute while the count of the radial was 120, thus showing the deficit of 40 beats. The lungs were clear and the liver edge was palpable and tender to pressure.

The electrocardiogram showed the auricle to be in flutter at the rate of 320 per minute, while because of a partial block of 2 to 1 the ventricular rate was 160 per minute (Fig. 9).

The tincture of digitalis in 30-minim doses every four hours was given, and two days later the auricles were in fibrillation, with a ventricular rate of 104 (Fig. 10). The digitalis was continued, and two days later the ventricular rate was 76 (Fig. 11). Because of the sense of nausea being rather severe he refused to continue the digitalis for four days, when the increasing commotion of the fibrillating ventricle caused him to be persuaded to try the tablet

of digipuratum, two tablets every four hours. The rate of the ventricle came down, and four days later the auricle became regular at 72 per minute, with the ventricular contraction following every beat at a time interval of 0.2 second (Fig. 12).

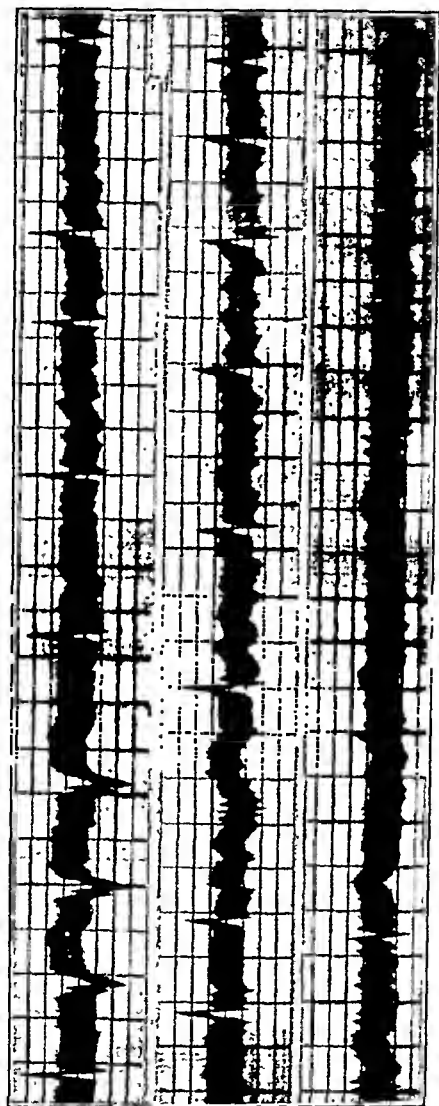


FIG. 10.—Case IV. O. C., taken February 19, 1916, shows fibrillation of auricle with ventricular rate of 104.

Many cases of flutter have been reported which have been changed to fibrillation, and subsequently, after slowing by digitalis, have resumed their normal sequential rhythm. This is the aim and hope of the procedure.

The employment of digitalis to effect the rhythm as shown in these cases should not permit us to forget that such use depends

on the accurate diagnosis of the condition. If there is doubt as to the cause of pulse frequency one should hesitate in the administration of such doses of digitalis, for the production of fibrillation

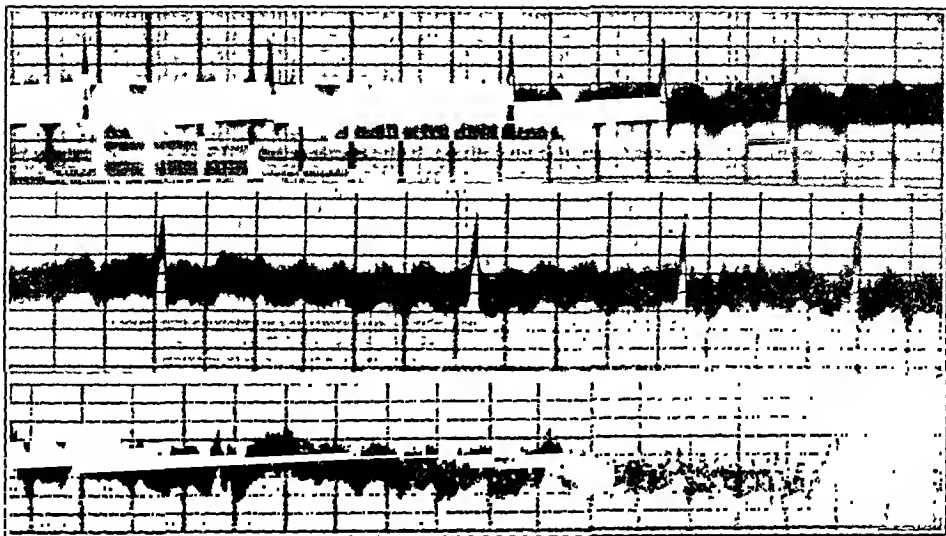


FIG. 11.—Case IV. O. C., taken February 21, 1916, shows fibrillation with ventricular rate of 90.

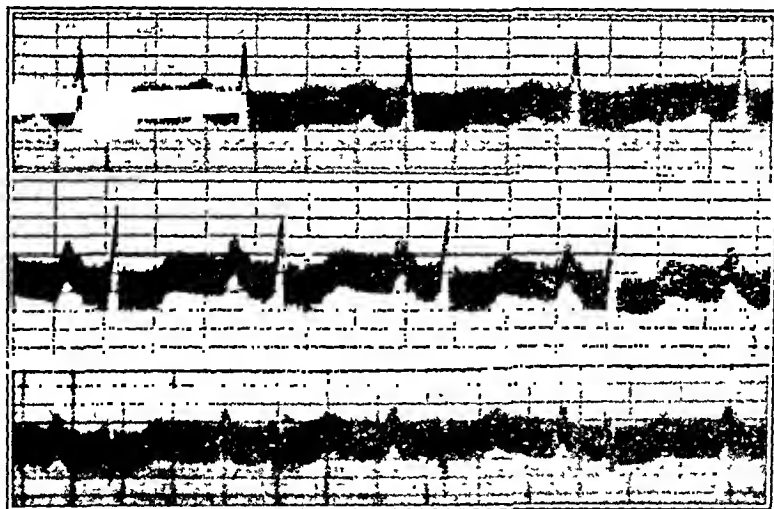


FIG. 12.—Case IV. O. C., taken February 29, 1916, shows sequential rhythm, with conduction time of 0.2 sec. *T*-wave in lead II downward. *S*-wave of lead III taken in conjunction with *R*-waves of leads I and II, showing hypertrophy of left ventricle.

in an otherwise healthy heart would not be desirable nor justifiable. With proper precautions we may draw the following conclusions:

1. The gross irregularity of the ventricle in cases with fibrillation of the auricle can be controlled by digitalis if sufficient drug is exhibited.

2. The patient should be instructed to continue the use of digitalis for the remainder of life, and should be taught how to determine the amount of the dose necessary from day to day to control the heart rate. Give sufficient drug to maintain the rate of the ventricle below 70 per minute when counted after a rest in the late afternoon.

3. The fibrillating auricle under a short course of digitalis may return to normal rhythm.

4. In auricular flutter the aim of treatment with digitalis is to produce auricular fibrillation and then control the rate of the ventricle with digitalis, hoping in the favorable cases for a renewal of normal sequential rhythm.

### SYPHILIS OF THE LUNG.\*

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CLAYTOR,<sup>1</sup> in 1905, made the following statement: "Whether we agree with the majority who hold that syphilis of the lung is rare in the adult, or with the few who consider it more common, we all must accept the opinion of the best authorities that the condition does exist. Now when it is taken into consideration that syphilis is curable and that the advanced cases of pulmonary tuberculosis, with which it is likely to be confounded, are as a rule, incurable, one should be all the more careful to make no mistakes." This in brief is the chief reason for reviewing the subject; not so much for the purpose of presenting a few cases that have perhaps some academic interest, but chiefly in the hope that by constantly bearing in mind that syphilis of the lung does occasionally occur, we may by correct diagnosis and intensive treatment save a life that might otherwise be lost. As Virchow<sup>2</sup> said: "Some patients die of so-called tuberculosis for lack of antisyphilitic treatment."

The question of its frequency or rather rarity is of some interest, in that considerable divergence of opinion has existed from time to time. This disagreement has not depended entirely upon the personal judgment of the individual author, but has reflected rather closely the development of clinical medicine.

**HISTORICAL.** A survey of the abundant literature can be conveniently divided into three historical epochs:

1. A long period, beginning with Paracelsus in 1500 and ending with Laennec in 1800.

\* Read before the San Francisco County Medical Society and before the University of California Hospital Medical Society.

2. The second period commenced with the pathological investigations of Depaul<sup>3</sup> and Virchow<sup>2</sup> in the first half of the nineteenth century and ended with the observations of such clinicians as Fournier,<sup>4</sup> Laneereux and Dieulafoy<sup>5</sup> at the beginning of the twentieth century.

3. The third period covers the last ten years, and includes the discovery of the *Spirocheta pallidum*, the complement-fixation test of Wassermann, the introduction of salvarsan by Ehrlich, and the extensive use of the roentgen rays in the interpretation of pulmonary disorders.

Fournier<sup>6</sup> speaks of the first epoch as the period of obscurity. These three hundred years included the most fanciful conceptions, utterly lacking in precision, unfounded in any accurate research. It sufficed in those days, for a pulmonary affection to follow a venereal infection, whether gonorrheal or syphilitic, for the pulmonary lesion to be declared of venereal origin. Cases were seriously reported in which the suppression of a gonorrheal discharge was followed by a so-called venereal phthisis, which in turn vanished upon the reappearance of the urethral discharge. In comparing the large number of cases of pulmonary syphilis reported during these three hundred years with the comparatively small number reported in the last one hundred years, the elder Fournier speaks of "the credulity of our fathers and the incredulity of our contemporaries." In fact, there existed in this older epoch absolute confusion, a few simply believing in a predisposition on the part of syphilitics to contract phthisis, while the greater number firmly believed in a real venereal phthisis, identical in signs and symptoms with all other phthises, but differing as to cause. Laennec, however, in differentiating pulmonary tuberculosis as a distinct disease, opened the way to the recognition of a true pulmonary syphilis.

The second period produced careful scientific investigations. First came the macroscopic observations of Depaul,<sup>3</sup> in 1837, of a condition in the newborn which Virchow,<sup>2</sup> in 1858, described histologically and called pneumonia alba. Subsequently the various forms in the adult were accurately described from a pathological stand-point, and probably we know but little more today of the picture at autopsy than was known fifty years ago. After the introduction of the stethoscope, and finally with the discovery of the tubercle bacillus, clinical observations became more precise and reliable. The general result of this scientific period was the conviction that pulmonary syphilis was a clinical entity, but that it was far less common than had been hitherto supposed. The only question in dispute was its actual rarity. Was it merely uncommon or was it really a rare medical curiosity?

In autopsies upon 97 cases of acquired syphilis, Chiari discovered one case of syphilis of the lung. Peterson,<sup>7</sup> in 88 autopsies of acquired syphilis, found 11 cases of pulmonary syphilis. In 1884 Hiller<sup>8</sup>

collected reports of 84 autopsies showing syphilis of the lung, but Councilman<sup>9</sup> regarded only 28 of these as definitely syphilitic. On the other hand, Fowler,<sup>10</sup> in searching through all the London museums, found only 12 cases, while in 1905 the Army Medical Museum at Washington, consisting of 13,000 specimens, did not contain one instance of this disease.

Certain groups of clinicians, however, considered the disease much more common than generally supposed. Satterthwaite<sup>11</sup> thinks that lung syphilis is greatly underestimated by the general practitioner and "almost unknown to many syphilographers." Pankritius,<sup>12</sup> who in 1881 wrote one of the most important monographs on the disease, with a very complete review of the literature, found it by no means unusual; likewise other German authors, as Schnitzler<sup>13</sup> and Grandidier,<sup>14</sup> and of the French clinicians, Fournier,<sup>4</sup> Lancereux and Dieulafoy.<sup>5</sup> On the other hand, clinicians of a more strictly pathological bias still insist upon the rarity of pulmonary syphilis. Thus Osler,<sup>15</sup> in twenty-five years' experience, cannot recall above half a dozen. Stengel<sup>16</sup> suggests that this difference of opinion depends largely upon the point of view of the observer, whether as a clinician or as a pathologist, the former believing that this condition is comparatively common, the latter that it is very rare. This may be due in part to the failure of the pathologist to recognize syphilis. It is by no means simple to differentiate between pulmonary syphilis and pulmonary tuberculosis not only at the bedside but in the pathological laboratory. As Claytor<sup>1</sup> says: "The only absolutely certain point of difference in many cases is the presence of the tubercle bacillus, and even this unquestionable evidence of tuberculosis does not preclude the possibility of associated syphilis. Pulmonary tuberculosis is so common, and syphilis of the lung thought to be so unusual, that it seems probable that some of these cases, because of their very rarity, may slip by with a diagnosis of tuberculosis. Many cases of supposed phthisis give such a typical history and show such characteristic signs of the disease that it does not seem necessary to examine the sputum, or even if the bacilli are not found on a few examinations no change in the diagnosis seems called for. The same line of argument is used in the post-mortem room. The condition is so much more likely to be tuberculous than luetic and so difficult to distinguish from it that it is almost always placed in that class unless pronounced syphilitic lesions of other organs are discovered." It may be mentioned again that this whole problem would merely resolve itself into the satisfaction connected with a correct differential diagnosis if it were not for the tremendous practical importance to the patient of such correct diagnosis.

When we come to consider the third epoch in our knowledge of pulmonary syphilis it would seem at the outset that a solution of the difficulties was at hand. But such is not the case. To my

knowledge, Schaudinn's *Spirocheta pallidum* has not been found in the sputum expectorated by pulmonary syphilitics, and would be with difficulty differentiated from the numerous spirochetes normally inhabiting the mouth. It likewise remains for someone to find these organisms with any frequency at autopsy in the lungs, as Warthin, for instance, found them in the myocardium. Such an investigation of a large series of autopsies upon syphilitics would, I think, go far to dispel the prevalent ideas as to the rarity of lung syphilis. It might have been expected that the Wassermann reaction would be of considerable assistance. But this is frequently not the case. Negative Wassermanns in syphilitics are by no means uncommon, and a positive Wassermann merely indicates that the patient has syphilis but not that the pulmonary condition is luetic. However, in those cases in which history signs and symptoms are all lacking, a positive test may at least lead to a suspicion that the phthisis has a specific etiology. It might have been hoped that the roentgen rays would give us some sort of characteristic picture which would permit of definite recognition. However, roentgenographs are disappointing in the sense that they do not provide us with an exclusively unique picture. But they are of value in a negative sense, for they decidedly help to exclude pulmonary tuberculosis. The roentgen-ray plate of a luetic lung is quite unlike that of a Koch infection, but it is not unlike many other pulmonary conditions, all of which result in peribronchial thickening. Gummata do present striking shadows, but have to be differentiated from malignant growths. We may conclude then that even today our knowledge of pulmonary syphilis and our ability to diagnose it leaves much to be desired.

**PATHOLOGY.** In a general sort of way one can classify the lesions anatomically into three groups:

1. The formation of gummata.
2. Those cases in which changes in the connective tissue predominate.

3. Those cases where alterations of the parenchyma predominate.

Combinations and modifications of these may occur, but the changes just mentioned represent the principal types of lesions in acquired syphilis of the lung.

The gummata may be single or multiple, vary in size and shape, and occur in any part of either lung. Some authorities have attached peculiar importance to the frequency of such gummata in the middle lobe of the right lung, and attempted to establish this point as a useful means of differential diagnosis. This does not seem entirely justified by a critical review of many cases recorded by many different authors; nor does it seem reasonable to suppose that this particular portion of the lungs should be a site of predilection, though it must be admitted that different bacteria select special organs with extraordinary constancy. The very fact that such a protean disease



as syphilis so rarely attacks the lung when spirochetes in large numbers must circulate through the lung in the blood stream is evidence enough of this selective characteristic. The gummata resemble those found elsewhere in the body and may readily be mistaken for tubercles. Though different details of the histological picture have been advanced as points of differentiation, the presence of the tubercle bacillus is the only final proof.

The second group comprises those cases in which fibroid induration is the outstanding feature. This is essentially a chronic process, and Pankritius considers this primary proliferation of the connective tissue in lung syphilis as characteristic of lues, for in other diseases of the lung which have hyperplasia of the connective tissue it is secondary to some primary condition, such as the chronic pneumonia of stonecutters and grinders. Virchow<sup>2</sup> considered the condition like the specific inflammations of the liver and testes.

The implication of the parenchymatous structures in lung syphilis was emphasized by Councilman.<sup>9</sup> This is essentially a pneumonia with fibrinous exudation.

**SYMPTOMATOLOGY.** The onset of pulmonary syphilis is very insidious, very slow, latent, and usually entirely ignored and unrecognized. Fournier compared it in its stealthy beginnings with the lack of symptoms from a gumma of the hard palate. The patient rarely realizes that there is anything abnormal in his mouth until perforation occurs and liquids regurgitate through his nose. This is in striking contrast to the rich and varied functional disturbances of a pulmonary tuberculosis at a similar stage of development. The symptoms of pulmonary tuberculosis are due to two causes: On the one hand tuberculous intoxication, upon which, for example, the anemia depends; on the other hand the symptoms due to reflex action of the pneumogastric (Pottenger), namely, cough, the tachycardia and gastric disorders, etc. And, moreover, these two disturbances, the general and the local, are usually associated. This is not the case in early pulmonary syphilis. The process must be far advanced before any change in the general health is noticeable. The patient preserves an appearance of strength, his complexion and color are good, his facies normal, his appetite remains, and he holds his weight fairly well. In fact, it is exceptional for syphilis to produce phenomena of general intoxication in any way comparable to the severity of the lesions from which the patient is suffering, even though these be enormous destructive ulcerations. Syphilitics do lose weight and appetite, become weak and enfeebled, but by no means to the same degree as would a tuberculous individual in the same stage of the disease. It is also worthy of note, according to Fournier, that whereas mediastinal adenitis is constantly present in early pulmonary tuberculosis, it is almost always absent in early pulmonary syphilis. This corresponds to the lack of regional adenitis in most tertiary lesions. As a result the reflex action of the

pneumogastric are not excited and the usual symptomatology of early tuberculosis does not occur. If cough does occur in an early pulmonary lues it is probably due to laryngeal, tracheal, or bronchial lesions. But as the gummata, fibroid or parenchymatous processes increase, functional disturbances will arise, and these are mostly dyspnea, cough, and expectoration.

Dyspnea is quite common. In some cases it may be due to a complicating stenosis of the bronchi or trachea. It is frequently very severe.

Neither the cough nor the sputum have anything characteristic about them. The cough is often spasmodic, like the dyspnea. The sputum may be little in amount, or very abundant, purulent, greenish, and of foul odor from bronchiectatic cavities. In an uncomplicated case, repeated examinations will consistently be negative for Koch's bacillus. Elastic tissue may be present from destruction of lung tissue. In fact, pieces of a gumma may be coughed up through a bronchus, as in the case reported by Cube.<sup>17</sup>

Hemoptyses are less common than in tuberculosis, probably due to the chronic obliterative endarteritis, but they do occur. Blood-streaked sputum is not unusual.

Night-sweats and pyrexia are the rule, though the fever seems to be more variable in character than in tuberculosis.

Loss of weight always follows as the disease progresses, but usually to a less degree than in tuberculosis. Emaciation is exceptional, but may be pronounced.

The physical signs are in no way characteristic, are identical, in fact, with tuberculosis. It is said that necrosis and softening is rarer in gummata than in tubercles, and it is the general opinion that cavities do not occur as frequently in lung syphilis; but cavities unless large are usually missed clinically or diagnosed when they are not present, so that this point will not be of much assistance in reaching a diagnosis. In a general way one might say that syphilis of the lung is more frequently unilateral, more often circumscribed, and does not show the same predilection for the apex of the lung as does tuberculosis. But all these points are of meager value in forming a conclusion, and it may be noted that recently Landis and Lewis<sup>18</sup> called attention to a latent type of pulmonary lues confined to the apices, in every way simulating early tuberculosis.

**DIAGNOSIS.** The Wassermann test, as said before, is helpful, if positive, in directing attention to the idea that the pulmonary lesion may be luetic, but merely signifies that the patient has lues; if negative it has no value one way or another.

Luetic lesions elsewhere or a clear history of primary secondaries or other luetic stigmata may make one suspicious.

There are really but three points in the diagnosis that seem to be of any help:

1. The absence of tubercle bacilli on repeated examinations.

2. The curious lack of proportion between the gravity of the physical signs, the severity of the symptoms, and the astonishingly good appearance of the patient.

3. Merely bearing in mind in the examination of every suspected pulmonary tuberculosis that there exists such a curable lesion as lues of the lung.

PROGNOSIS. Balzer<sup>19</sup> said, rather neatly, that the prognosis for a patient suffering from lues of the lung depended upon the intuition or clairvoyance of his physician. If the condition is recognized the treatment is simple, startling in its results, in some cases almost miraculous. Even patients that have been reduced to a state of great enfeeblement and cachexia, whose condition would appear to be desperate, are restored to normal in an astonishingly short time. To be convinced of this one need but read some of the cases so dramatically described by Fournier, in which the cures were quite spectacular. Our results today should be even more brilliant, for with the wider adoption of accurately controlled mercury injections, instead of haphazard inunctions\* or mouth medication, and with the addition of salvarsan we have more powerful remedies than did Fournier. There is no necessity for considering the treatment. It is simply the intensive treatment of syphilis, consisting of intramuscular mercury salicylate injections, intravenous old salvarsan, and large doses of potassium iodide. Salvarsan seems to be specially prompt and efficient in this condition.

If the disease is not recognized death will result in the majority of instances from general weakness or lesions in other viscera. Pulmonary syphilis develops slowly, much more slowly than tuberculosis, though cases like "galloping consumption" have been reported. A few cases will undoubtedly regress spontaneously without any treatment, as is characteristic of syphilitic lesions elsewhere. Lung syphilis may open the door to pulmonary tuberculosis and thus cause death indirectly, and this leads to a brief consideration of the association between these two diseases.

ASSOCIATION WITH TUBERCULOSIS. When the frequency of lues of the lung is brought up for discussion, generally the first remark made by those who are very conservative is this: Syphilis and pulmonary tuberculosis are both extremely common; is it not to be expected that both may frequently coexist in the same individual? Why, then, when pulmonary lesions develop in a syphilitic should one be suspicious of syphilis of the lung when pulmonary tuberculosis is incomparably more common! This reflection is not only correct but is supported by the well-recognized fact that the congestion, erosions and ulcerations of the mouth, pharynx, larynx and trachea, so common in secondary syphilis, actually predispose

\* Mercurial inunctions properly and conscientiously administered by a nurse or attendant, are potent and efficient. Objection is raised above to the "rubbing" done by the average patient at home.

to the development of consumption. Laryngologists have repeatedly warned us of this possibility. Though the laryngitis is syphilitic at the outset a tuberculous process is sometimes engrafted upon it, and though specific therapy will cure the syphilitic lesions the tuberculous laryngitis remains. Potain<sup>20</sup> likewise called attention to the probability that the syphilitic bronchitis, so common in the secondary stage, may in a similar manner open the door to the tubercle bacilli.

Syphilis of the lung and tuberculosis of the lung may occur together, and in those few cases in which this simultaneous involvement has occurred, antiluetic treatment would seem to have cured the syphilitic lesions, while the tuberculous portion continued to develop.

The association of pulmonary tuberculosis and syphilis (I am referring now to syphilis in general, not lung syphilis) may obviously take place in two ways: a tuberculous individual may acquire syphilis or a syphilitic may become infected with pulmonary tuberculosis. When syphilis attacks a patient already ill with consumption the pulmonary tuberculosis is aggravated and pursues a more rapid course.

When tuberculosis appears in a syphilitic the development of the tuberculosis would seem to depend upon the interval that had elapsed since the primary lesion, the chancre. In other words, when tuberculosis is added to an active, recent virulent syphilis the tuberculosis pursues a more rapid march, the co-called galloping type. Chretien<sup>21</sup> injected two guinea-pigs with the blood of syphilitics in the secondary stage and then inoculated them with tubercle bacilli. These pigs died much sooner than the control pigs who had merely been inoculated with the tubercle bacilli. Though not to be regarded as experimental proof, still this observation is in accord with clinical experience.

But when tuberculosis develops in a patient whose syphilitic infection occurred over six years before, the tuberculosis pursues a mild, slow course without pyrexia and tending to the chronic fibrous type. Stieffel<sup>22</sup> assembled some statistics which demonstrated this point quite strikingly, the longer the interval after the chancre the milder the tuberculosis.

**ABSTRACT OF CASES.** CASE I.—The first patient was a married man, aged thirty-eight years, who came to the out-patient department of the University of California in August, 1914.

*Family and Marital History.* His family history does not concern us except to note that there was no history of tuberculosis. He reported his wife in good health, likewise his two children; no misadventures.

*Past History.* Two years before coming to us he had a lump on his right parietal bone, which was removed. Wassermann at this time was negative. He probably had his initial lesion sixteen years

before, though he spoke of it as a soft chancre; no history of secondaries; no antiluetic treatment. Otherwise his past history is unimportant.

*Present Illness.* Two years before we saw him the patient began to cough, apparently a dry irritative cough, without expectoration. During this time he was a street car conductor and thought that the fog and night air caused the cough. One year ago while working at night as a guard at San Quentin prison, his present occupation, the cough began again; no hemoptyses or sputum. He had pleurisy twice on his right side during this time, without effusion. (It might be said in passing that some of these so-called right-sided pleuritisies

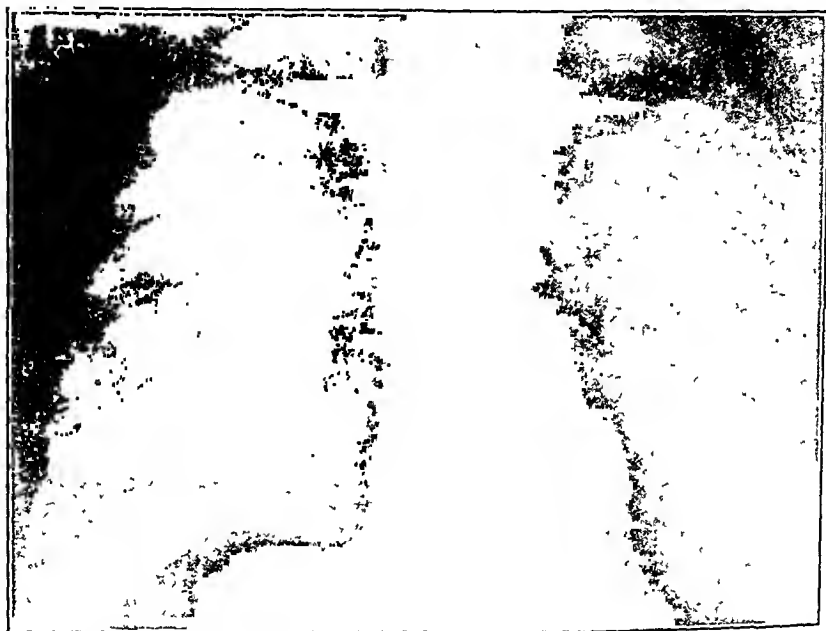


FIG. 1.—Roentgenogram of Case I, taken before treatment. Extensive dense root shadows and diffuse peribronchovascular thickening extending well out to the pleura.

in luetics are caused by a periphlepatitis.) He then began to lose weight and strength, felt tired constantly, and during the three weeks previous to August, 1914, suffered from drenching night-sweats. The patient lost thirty-five pounds during this last year. In this case there was no sputum to examine.

*Physical Examination.* The patient was by no means emaciated despite this great loss of weight. On the contrary he was a large, muscular man, and the weight he lost was probably surplus fat. He looked well, was well nourished, and did not give the impression of being afflicted with a severe illness. A depression was noted on the right parietal bone, the site of the excised lump previously mentioned. Otherwise no evidence of past or present lues was discovered.

His lungs were likewise almost normal, slight narrowing of the right apex, with harsh breathing, being the only abnormality. His roentgen-ray plate is shown in Fig. 1. The Wassermann, August, 1914, was positive, three plus.

Since he resided at San Quentin and could not come with great regularity our routine therapy was not employed. He received nothing but four full doses of Old Salvarsan intravenously in the course of the following six weeks. August 21 his weight was 172 pounds, a gain of 20 pounds. His night-sweats disappeared permanently two days after the first salvarsan; his cough was markedly ameliorated and ceased entirely after the second salvarsan. After the last salvarsan he remained away, feeling too well to return, so one year later, October 3, 1915, I went over to San Quentin to see him and found him in robust health, having gained 30 pounds more, so that his weight was 220 pounds, 50 pounds more than before treatment. He has not had any return of his cough or night-sweats.

**CASE II.**—The second patient was a young married woman, aged twenty-two years. No family history of tuberculosis. She had been married twice; no pregnancies during her first marriage; she married her second husband one and a half years ago, had one three months' miscarriage, and a child, who is now eight months old, apparently well with no stigmata of congenital lues and with a negative Wassermann.

*Past History.* This contains the following item of interest. Two and a half years ago, during her first marriage, she became blind for two months, and her physician gave her an injection into the left buttock which cured her blindness but resulted in an abscess. This is not absolute evidence of syphilis by any means, but it does raise the suspicion of aluetie iritis cured by an intramuscular injection of salvarsan. She has no knowledge of a primary lesion or of a secondary manifestation.

*Present Illness.* She came to the clinic in September, 1915. Six weeks previously she had a hard cold with fever and chills, was sick in bed two days, coughed, and raised abundant quantities of thick yellow, bloody sputum. She had night-sweats then. The cold continued, and during the month before we saw her, grew worse. She lost her appetite, became increasingly weak; suffered greatly from dyspnea and daily chills and fever, and had spasmodic coughing spells, when she could not stop coughing for half an hour. During these six weeks she lost 6 pounds, 13 pounds in the previous three months, prior to September. She began to have pains in her chest on both sides, of pleuritic character. No hemoptyses.

*Physical Examination.* The patient made a curious impression. She looked ill; her face was flushed; her temperature was 103°; pulse 130; respirations 60 to the minute; had frequent violent spells of coughing, very exhausting, which interrupted the examination for several minutes on several occasions. And despite all this she

was by no means emaciated. She was slender, perhaps, and weighed 125 pounds. Supra- and infraclavicular fossæ were well filled out; her chest was well formed. Excursion of the lungs was very limited on both sides. There was dulness at both apices, front and back, more marked on the left, and the percussion note was impaired over both lungs over the entire back. The breath sounds were very harsh and coarse, approaching bronchial breathing, with coarse bubbling rales, especially on the left. A friction rub could be heard in both axillæ, and the patient complained of great pain on taking a

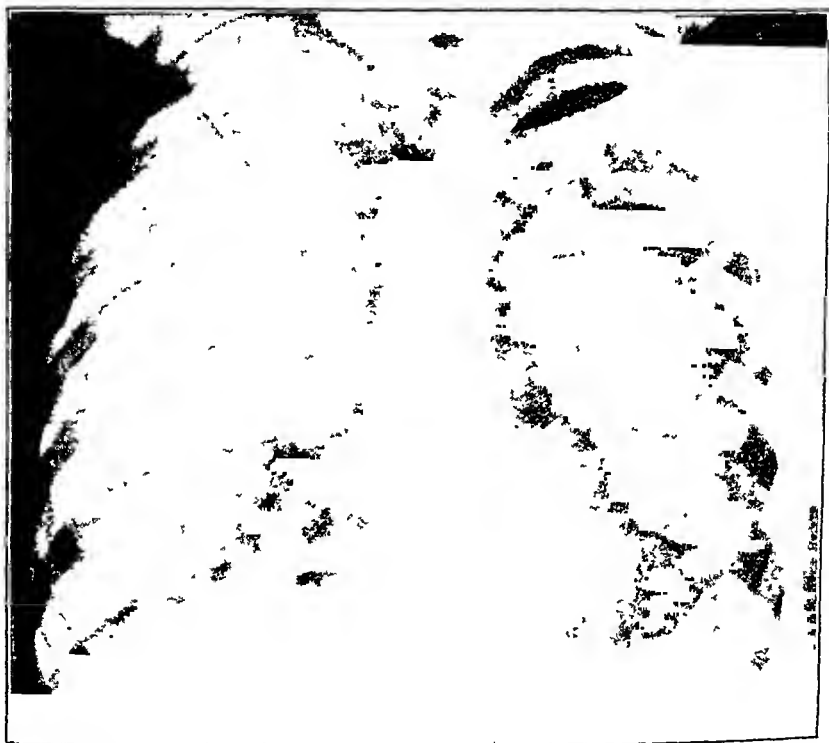


FIG. 2.—Roentgen-ray plate of Case II, taken before treatment. There is an area of increased density in the cardiohepatic angle consisting of coarse masses along the descending trunks of the right bronchus.

deep breath, worse on the right; no effusion. She expectorated much thick mucopurulent sputum streaked with blood. Repeated examinations failed to reveal tubercle bacilli. Her roentgen-ray plate is shown in Fig. 2. Her Wassermann was positive one plus. Otherwise the physical examination was negative.

There was nothing here to suggest pulmonary lues, but two points were suspicious: (1) The absence of tubercle bacilli in a sputum that looked as though it would be loaded with them. (2) The curious inconsistency between the severity of her symptoms and signs and

her healthy physical appearance, and perhaps also the history of blindness cured by an intramuscular injection. She was given potassium iodide at once and an intragluteal injection of mercury benzoate. Three days later she was decidedly better; temperature had fallen from  $103^{\circ}$  to  $100^{\circ}$  and the pulse from 130 to 92. She coughed less and had no more violent spasms of coughing; her dyspnea had diminished. Two weeks later her temperature was normal, and pulse 80. She was still coughing and her night-sweats continued, but were less severe. We began then very carefully



FIG. 3.—Same patient as Fig. 2, taken during treatment. Marked clearing of right base in cardiohepatic angle, with reappearance of the normal bronchial markings.

with old salvarsan intravenously, the first dose being 0.1 gram, the second 0.2 gram, the third and fourth 0.3 gram. In addition she received four mercury benzoate and four mercury salicylate injections and potassium iodide continuously.

December 16, 1915, one month after ceasing treatment, the temperature and pulse were normal; no dyspnea; no sputum; no more night-sweats; no more cough; no more pains in her chest; had worked part of the time in the moving-picture business, which required her to be in swimming frequently. Examination of her lungs at this time shows no wasting of intercostals or shoulder



muscles; no spasm or tension anywhere; diminished resonance above the second rib in front on both sides; slight dulness above on the right. Breath sounds slightly harsh over the hilus on each side, a little worse on the left; no rales. Expansion in general is a little slow; filling slightly labored; the breathing of diminished elasticity. A series of three roentgen-ray plates taken before, during, and after treatment are shown in Figs. 2, 3 and 4, and show quite clearly the improvement that took place. She gained 15 pounds in weight, from 125 to 140 pounds, the highest she has ever weighed.

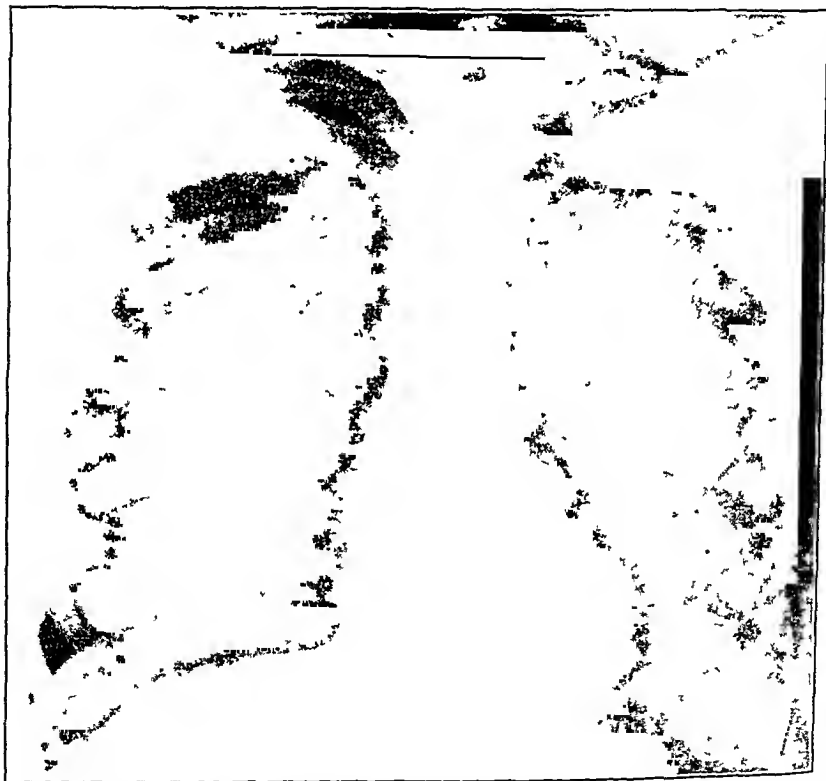


FIG. 4.—Same patient as Figs. 2 and 3 after treatment. Further clearing of right base, cardiohepatic angle well marked, bronchial markings in this area further reduced in size and density.

CASE III.—This patient, a young married woman, aged twenty-six years, was delivered at seven months of a premature baby at the University of California Hospital in January, 1915. The baby lived only a few hours. The Wassermann of the mother proved to be very strongly positive. She was accordingly referred to the medical clinic for antiluetic treatment.

She then gave the following history: Her primary lesion just inside the vulva occurred in December, 1913, followed by inguinal

adenitis, but no other signs of secondary invasion. She received at once twenty mercury injections from her private physician. Shortly after becoming pregnant her Wassermann was strongly positive, and she received from another physician one injection of old salvarsan and mercury pills and injections for one month, which antenatal therapy proved entirely inadequate.

On examination, February, 1915, the following points of interest were noted: cyanosis, dyspnea, precordial pulsation, presystolic thrill palpable over apex and base, culminating in a forcible shock corresponding to the first sound. Percussion and auscultation confirmed the diagnosis of a typical mitral stenosis. In addition there was a diastolic blow heard down the left side of the sternum, loudest at the pulmonic area. In the absence of peripheral signs (Corrigan pulse, high pressure, pistol-shot sound, etc.) it was finally decided that we were dealing with a Graham-Steele murmur, a relative pulmonary insufficiency. The heart was considerably enlarged to the left and right especially in the region of the left auricle and right ventricle. A history of acute tonsillitis as a child, complicated by chorea seemed sufficient cause for the cardiac picture.

Treatment was accordingly begun but was necessarily handicapped so far as the administration of salvarsan was concerned by reason of the cardiac complication. However, she received twelve mercury benzoate injections of mild dosage and small doses of potassium iodide over a period of four months, by no means satisfactory. In July, 1915, after having remained away for two months without treatment, she received 0.2 old salvarsan. A roentgen ray of her chest was taken at this time (Fig. 5) and revealed a mass roughly the shape and size of a large lemon, apparently in the lower lobe of the right lung. This was assumed to be a gumma. She returned to us in November after an absence of three months. She then admitted occasional night-sweats but no cough, and her dyspnea seemed well accounted for by her valvular disease. Another roentgenogram of the chest at this time disclosed precisely the same shadow in the same position and of the same size. Her Wassermann was then positive, one plus. From December, 1915 to April, 1916, she received twelve mercury salicylate injections and moderate doses of potassium iodide. During January and early February she coughed severely, especially at night, and suffered from drenching night-sweats. The antiluetic treatment did not influence this pulmonary affection, and finally inhalations and an ordinary cough mixture had to be utilized before recovery took place. By the end of February her cough and night-sweats had ceased. In April she had another attack of "bronchitis" (?). Sputum on both occasions was devoid of blood or Koch's bacilli. Finally, in May, 1916, another roentgenogram of the chest was taken, and again demonstrated an unchanged shadow in the right lung. This shadow has persisted therefore (known to us) for ten months, but it must be

confessed that, for various reasons, the therapy has been far from intensive and effectual. Her cardiac condition having improved considerably we are now attempting large doses of potassium iodide from 100 to 150 grains per day and salvarsan in an effort to dissolve this gumma, if such it be.

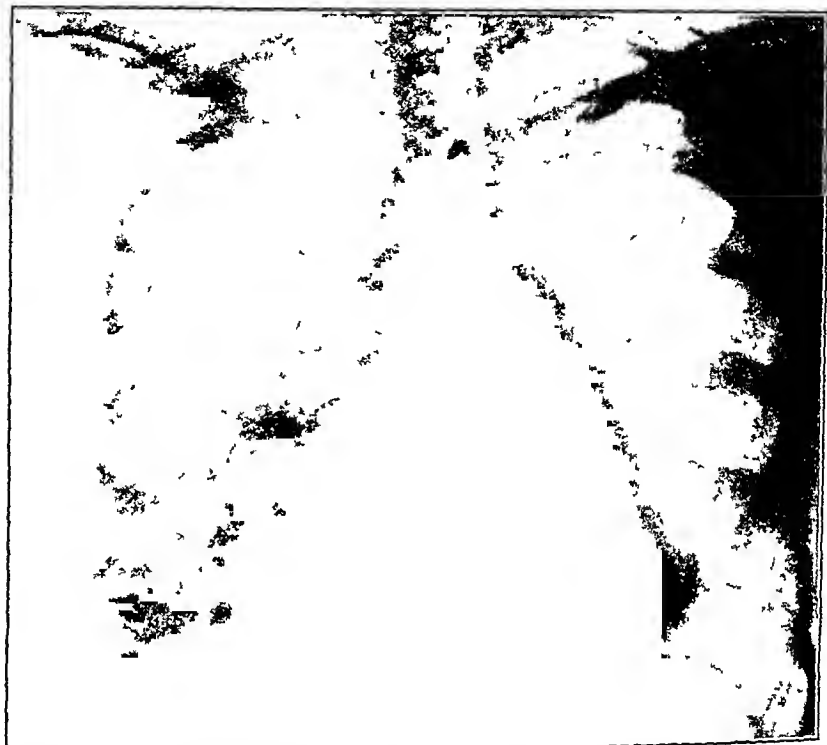


FIG. 5.—Roentgenogram of Case III before treatment (roentgen appearance unchanged after mild therapy). Circumscribed area of increased density at the right hilum, 3 by 6 cm., of uniform intensity, with sharply outlined margins; increased bronchial markings to the right base gumma. Note enlarged mitral heart

CASE IV.—(Reported through the courtesy of Dr. Rene Bine). This patient, a man, aged forty-one years came to Dr. Bine's office, July 7, 1915.

His family history is not significant. He had been married eighteen years; reported his wife in good health; had one son, aged sixteen and one-half years; alive and well; no dead children and no miscarriages.

*Past History.* Fifteen years ago had a small tumor cut out of right cheek, leaving now but a small dimple as evidence. Before he married was treated for some swelling around eyes. Also had a small opening on right side of neck just above sternoclavicular joint and this discharged pus. After awhile this stopped, then his nose got stopped up. This nasal trouble has been present now five

or six years. Seven and one-half years ago had inflammatory rheumatism, was four weeks in bed. Malaria twenty years ago; no typhoid. He denied both lues and gonorrhea.

*Habits.* Does not use alcohol or tobacco. Appetite normal; sleep normal; bowels regular.

*Present Illness.* Has been feeling run down for about one year. Has lost about 7 pounds. Has a slight cough but no sputum.

*Examination.* Well developed, poorly nourished, very pale looking, lower lids puffy; conjunctiva pale. Pupils normal, no enlargement of epitrochlears. Moderately enlarged inguinals. Postcervicals not enlarged. There is an enlarged gland on right side just below jaw; there is also a fairly marked swelling just above the left sternoclavicular junction. From this at the lower end, right over the sternum there is a little sinus from which a little pus can be squeezed out. A probe introduced into this area goes upward and outward into the soft tissues, apparently the seat of the swelling, and does not come in contact with any bone. Opening of this sinus is just opposite a scar of the previously healed one.

Heart: negative. Lungs: marked dullness from apex to fourth rib on right side and corresponding dull area posterior, being down to midway between the angle and the spine of the scapula. Breath sounds are harsher over dull area and voice sounds definitely increased. Lower borders of lung move normal on both sides. No rales. Abdomen: fairly full, nothing abnormal detected. Knee-jerks present and lively. Palate: there is marked perforation in the anterior portion of the palate; it was so far forward that it was almost overlooked. Nose: there is considerable swelling in the cartilages, breathing is probably greatly obstructed; the swelling is more marked on the right side of the septum. Blood: hemoglobin, 70 per cent., 3,750,000 reds, 8200 whites; polymorphonuclears, 62 per cent.; mononuclears, 3 per cent.; lymphocytes, 32 per cent.; eosinophiles, 1 per cent.; basophiles, 1 per cent.; transitionals, 1 per cent. Urine: negative. Wassermann, three plus. Pus from sinus shows many staphylococci, many polymuclear leukocytes, but no acid-fast bacilli.

From July, 1915 to March, 1916, he received thirty-two mercury salicylate intramuscular injections and 0.45 gm. neosalvarsan intravenously. He improved rapidly, the cough disappearing very soon. April 28, 1916, his Wassermann was negative; the patient felt entirely well and had more than regained his weight; in fact, he looked like a different man. The dull area from the right apex to the fourth rib had not cleared entirely, but was somewhat modified, while the sinus of the neck had healed completely. In this case the diagnosis and consequent successful therapy was due in large degree to a somewhat peculiar intonation of the patient, which prompted Dr. Bine to recall the patient just as he was about to leave the office, with the important result of finding the perforation

of the palate which as noted was unusually far forward. This discovery at once established the diagnosis of syphilis and aroused the suspicion that the pulmonary lesion might likewise be of luetic origin. Unfortunately no roentgen rays of the lungs were taken.

CASE V.—Woman, aged twenty-seven years. She had been married thirteen years; has three boys living and well (not examined); one child died, aged eight and a half years, of "typho-pneumonia;" another child died, aged one and a half months, of intestinal obstruction; no spontaneous miscarriages.

March, 1915, a luetic condition of the septum and soft palate was diagnosed; Wassermann strongly positive, and she admitted a sore on her vulva twelve years before. She was given mercury inunctions and later "mixed" internally, and the above process yielded promptly to treatment. The following November she developed her pulmonary affection. She insists that she never had any respiratory complaints previous to this date. Her symptoms at this time consisted of coughing, mostly at night and in the morning, with copious expectoration of purulent sputum. In the morning she would cough up a small glassful of sputum. She thinks she had fever; no night-sweats. After a severe spasm of coughing, she had a small hemorrhage. She was then referred by her physician to the University of California Tuberculosis Clinic, and diagnosed pulmonary tuberculosis, until examined by Dr. Lewis S. Mace, who referred her promptly to me with the following report:

"Little in chest except possible dilatation of bronchi above the hilus on the right, also some loss of elasticity; no active lung inflammation; careful examination of the sputum is negative for tubercle bacilli." January 17, 1916, when she reported to the medical clinic, her Wassermann was positive, three plus. Roentgen ray of the chest (Fig. 6) showed no evidence of tuberculosis, but marked thickening at the roots with peribronchial infiltration.

Examination showed a somewhat undernourished woman, apparently not very ill; weight 110 pounds. In the left frontal region a depressed scar was found, the result of a mass that had been incised August, 1914, probably a gumma. Otherwise, with the exception of the lungs as noted above, the entire physical examination was negative.

From January 27, 1916 to August 22, 1916, she received twenty mercury salicylate, 20 per cent., intramuscular injections and small doses of potassium iodide and 0.2 gram old salvarsan. She was unable to pay for further salvarsan therapy. Her cough cleared up rapidly, but she continued to expectorate two or three times a day a semipurulent sputum. This was repeatedly found negative for tubercle bacilli. By June 5, 1916, coughing had ceased entirely, and there was no longer any expectoration. Another roentgenogram was taken at this time, but is not reproduced because it shows precisely the same condition as before treatment, yet clinically the

patient is entirely well, no longer coughs or expectorates, and has gained 16 pounds. August 19, 1916, Dr. Mace examined her lungs at my request in order to compare her condition with his findings of January, 1916 (before therapy was begun) and reports as follows: "She has made a remarkable recovery and is a very different-looking person from the one who came to the tuberculosis clinic December 31, 1915, and was diagnosed pulmonary tuberculosis. No cough and no expectoration for the past three months. Percussion resonant throughout. Right side vesicular throughout. Left shows sharp

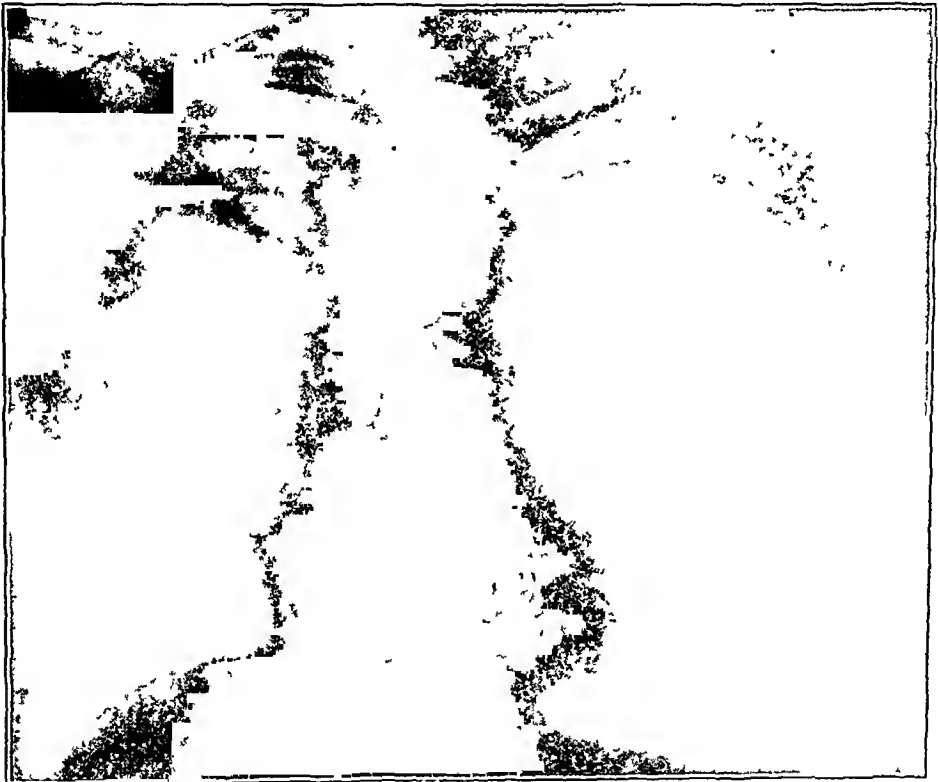


FIG. 6.—Roentgenogram of Case V (roentgen appearance the same before and after treatment). Dense mass of glands at the left hilus and generalized peribronchial thickening; slightly increased density at the right top.

breathing at the hilus, but no rales even on forced respiration or coughing. The above examination shows no abnormalities except slight rough inspiration at bases."

It is difficult to account for this improvement, under purely anti-syphilitic treatment, unless the pulmonary condition be considered luetic. It is certainly not tuberculous.

CASE VI.—A Russian housewife, aged thirty-five years, entered the University of California Hospital, November 19, 1915 (service of Dr. Herbert Moffitt). At this time she suffered from a gumma of her upper lip, and a lesion the size of the palm of the hand, kidney-

shaped, with area of necrosis and exudation of pus, and raised infiltrated edges and raw ham-colored periphery covering the lower end of the sternum. The soft palate was scarred and distorted from former lesions; the uvula practically gone, its remains scarred and drawn posteriorly. In short, she showed the characteristic late tertiary skin lesions of syphilis. The spleen was very large, hard, and firm, with rounded edge. The sharp edge of the liver could be easily felt and the right lobe extended to the iliac crest, with sharp, notched edge, but smooth surface. Fingers of both hands were clubbed and roentgen ray of left tibia and fibula showed periostitis. The patient had lost 70 pounds during the previous four years. Both Wassermann and luctin tests were strongly positive.

She remained in the hospital twenty days and received during this time three intragluteal injections of mercury salicylate and 1.1 gram old salvarsan in two doses; also potassium iodide. At the date of discharge all external lesions had healed, and the liver had diminished markedly in size.

It is to be noted that her lungs at this time were resonant throughout, bases moved freely, breathing was normal, and there was no fluid in the pleural cavities.

The patient left the hospital December 8, 1915, with instructions to report to the out-patient department for further antiluetic treatment, but she felt too ill and weak to do so. She reentered the hospital March 22, 1916, and during the three months' interval had lost 20 pounds more. She insisted that she took potassium iodide regularly during this time. Soon after leaving the hospital in December she noticed that her abdomen was swelling, which had gradually progressed. She had frequent attacks of abdominal pain, and was confined to her bed most of the time. She thought she had fever every morning; often was chilly, followed by sweats; occasional cough; no sputum. Wassermann was still positive three plus.

In addition to the smoothly healed lesions, treated during her previous entry, the following remarkable points were noted.

Chest: very thin, retracted spaces; prominent ribs. Left base moved much less than right. Intercostal spaces sucked in with respiration, especially at left base in front and in axilla. Respirations slightly increased in frequency and breathing harsh. There was consolidation of the lower lobe and the base of the upper lobe on the left, with fluid at the base. Bronchial breathing heard over all of this area with bronchophony extending high in the left axilla; crepitant and crackling rales heard above with moist rales at base on left. Few scattered crackles throughout both lungs, with harsh breathing. Shifting dulness elicited in front at the level of the fourth and fifth ribs on the left. Heart evidently pushed over to the right.

The abdomen was even more astonishing. It was rounded, bulging, fairly tense, and much increased over former entry. No shifting dulness or fluid wave could be elicited. The spleen was enlarged, much as before, with firm, round edge. The liver seemed to be much smaller than before treatment, but was difficult to feel. In the left flank a firm, tense, somewhat elongated mass, slightly movable, but apparently deeply fixed, was felt. This mass of enormous size was not present four months before. Since we are primarily interested in the pulmonary affection, suffice it to note that when she left the hospital, two months later, after intensive antiluetic therapy, this great tumor was practically gone, barely noticeable in comparison to its former size.

Two days after admission an exploratory puncture of the left thorax resulted in the withdrawal of 30 c.c. of a bloody fluid; upon centrifugalizing the fluid red cells settled out and a dark straw-colored fluid resulted in which a slight coagulum formed on standing; Rivalta, negative. Cells: great many red cells, with considerable emutation. Polymorphonuclears, 53 per cent.; lymphocytes, 26 per cent.; endothelial or tissue cells, 21 per cent.; apparently considerable degeneration of cells.

Four days later, thoracentesis was performed, the needle being inserted in the ninth space on the left side in line with the angle of the scapula and also in the eighth space in the left posterior axillary line; 200 c.c. of red bloody fluid was withdrawn. With deep breathing the lung descended against the needle above and with respiration a resistance inside needle toward the spine was felt. Signs remained about the same after tapping. Rivalta negative and cells as described above. The following day a roentgen ray of the chest was taken (face up), and as seen in Fig. 7 a shadow involving the entire left chest, especially dense at the base, is noted; heart displaced to the right. She was then given 0.6 salvarsan intravenously and placed on mercury inunctions and potassium iodide. April 1, three days later, the mass in the left lower abdomen was noticeably smaller, but the lung signs remained much the same. Her temperature had been normal and remained so throughout her two months' stay in the hospital.

April 6, it was noted that her back at the lower left base was board-like in consistency; that the whole left chest in the back was larger than the right, and that an area of bronchial breathing could be heard below the angle of the right scapula.

April 14 a needle was inserted in the tenth interspace in the line with the angle of the scapula on the left side; 1000 c.c. of dark brown fluid with bloody tinge was withdrawn. Specific gravity, 1020; Rivalta, negative; albumin, 4 per cent. Many red cells; practically all other cells are small lymphocytes.

The following day 0.4 gram old salvarsan was given intravenously. April 23, eight days later, dulness was receding in front and the



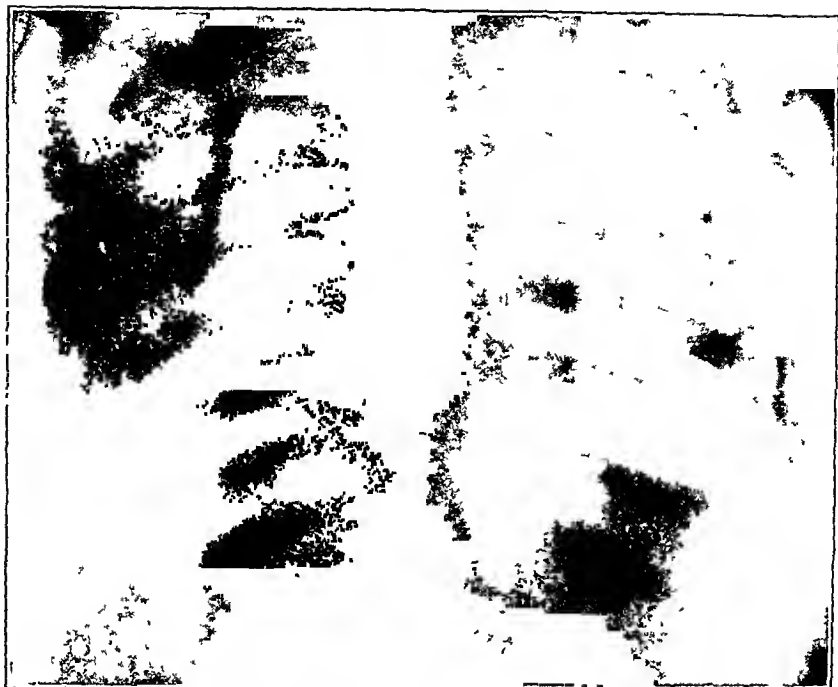


FIG. 7.—Roentgenogram of Case VI, taken before treatment (viewed from behind). Left chest entirely obscured by a diffuse shadow suggesting fluid. Heart displaced to the right; high diaphragm on the right; slight thoracic scoliosis.



FIG. 8.—Roentgenogram of same patient as Fig. 7, taken after treatment. Left lung field entirely clear; heart in normal position; right diaphragm now normal.

tubular quality of breathing had practically disappeared. The left base behind was still bulging and filled out, as if from fluid.

April 28, 0.6 gram arsenobenzol was administered intravenously. The iodides had to be discontinued April 8 because of marked iodism. Mercuric inunctions were given daily throughout her stay in the hospital.

By May 3 dulness at the left base was much reduced, with still some signs of fluid; no bronchial breathing. May 10 thoracentesis resulted in only 30 c.c. of fluid. The puncture was made not because there were any indications of much fluid but for diagnostic purposes.

A roentgenogram of the chest was taken immediately, and as seen in Fig. 8 the left lung had cleared remarkably; no indication of fluid; considerable peribronchial thickening in both lungs, with large shadows, probably glands at the hilus. The patient received 0.4 gram arsenobenzol May 20 and left the hospital May 27. At this time Dr. Whitney made the following note: "The lungs seem entirely clear, but there is a little dulness at the left base, probably thickened pleura. This has been a very remarkable case. It seemed hardly possible that the enormous mass in the belly and the practically solid lung could be syphilitic. The preliminary diagnosis was sarcoma. The remarkable clearing on mercuric and salvarsan seems to certify the syphilitic nature of the lesions."

The patient never coughed during the stay in the hospital, nor was there at any time any sputum to examine. Repeated blood examinations showed a marked secondary anemia: hemoglobin (Dare), from 30 to 45 per cent.; red cells, 2,400,000 to 3,136,000. The white cells varied from 4600 to 9100. The polymorphonuclears from 74 to 85 per cent.; platelets 152,000 to 192,000.

CASE VII. No. 25262.—A German, unmarried, aged thirty-six years, came to the medical clinic of the University of California Hospital July 27, 1916, complaining of cough. His family history and past history are of no significance. He denied venereal disease and no history of secondaries could be elicited.

His illness, which consisted purely of coughing with copious mucopurulent expectoration, dated from a month and a half previous. He had no fever, night-sweats, chest pains, or hemoptysis. He had lost 25 pounds during this time, weighing 155 pounds August 1, 1916.

Examination showed a strongly built, moderately nourished man, looking somewhat older than stated age. Pharynx disclosed a number of grayish ulcers, with slightly raised borders, surrounded by a reddened areola. There was general glandular enlargement: cervical, axillary, epitrochlear, and inguinal. There were squeaky inspiratory and expiratory rales over both sides, with possibly diminished resonance over both apices behind, but without further signs. Otherwise the routine physical examination was quite negative.

Roentgenogram of the chest (Fig. 9) showed what was at first interpreted as an "old central TB."

Sputum was examined on several occasions without finding any bacilli of Koch.

Wassermann in blood serum positive two plus, denoting a definitely positive test.

Antisiphilic treatment was begun at once, consisting of weekly injections of 20 per cent. mercury salicylate, potassium iodide, gr. 25 t. i. d., and intravenously arsenobenzol. One week after the first mercury salicylate injection he had gained 7 pounds and the cough had almost disappeared, sputum less, and only an occasional rale discoverable. In the first two weeks of treatment before giving arsenobenzol he gained 18 pounds, felt "new altogether," and



Fig. 9.—Roentgenogram of Case VII (roentgen appearance same before and after treatment). Diffuse peribronchial thickening. Note lengthened aorta.

certainly looked like a different man. From August 1 to October 25 he received ten mercury salicylate injections, potassium iodide, and three full doses of arsenobenzol. His weight was 155 pounds August 1; it was 190 pounds October 27, a gain of 35 pounds. His cough has disappeared, and consequently his sputum; and his chest is clear. Yet, another roentgenogram of his chest, taken October 13, shows no change from the picture seen in Fig. 9.

This case resembles Case V in several particulars. Both were considered tuberculous; both had negative sputa; both had positive Wassermann; both made remarkable clinical recoveries under anti-siphilic treatment, in the disappearance of both signs and symp-

toms; both show a roentgen-ray picture after treatment, indistinguishable from the picture taken before treatment. Are the shadows on the plates, scar tissue, the result of healing a syphilitic lesion? When a luetic ulcer of the skin is cured a scar remains. It is the scar-tissue contraction of a healed syphilitic stomach which often requires operative interference to restore function completely. Possibly this is the explanation for the persistence of roentgen-ray shadows after the symptoms have vanished, of which they were supposed to be the cause. If such be the correct interpretation it would be unreasonable to expect a perfectly clear plate after treatment.

CONCLUSIONS. 1. Syphilis of the lung is uncommon, but not extremely rare.

2. It is worth diagnosing correctly.

3. It does not produce a typical clinical picture, easy of diagnosis.

4. It should be kept in mind and ruled out in every case thought to be pulmonary tuberculosis where the sputum is negative for tubercle bacilli.

5. Proper antisyphilitic treatment produces remarkable cures.

6. Dr. Barker's advice is helpful (if you have a reliable serologist): "When in doubt, have a Wassermann test made; when not in doubt, still have a Wassermann test made."

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### THREE CASES OF INFECTION OF THE UPPER RESPIRATORY TRACT WITH STAPHYLOCOCCUS PYOGENES AUREUS, PRESENTING THE SYMPTOM-COMPLEX OF ACIDOSIS.

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DURING the winter of 1915 and 1916 in Boston and its vicinity the usual epidemic of "colds" was of such uncommon severity as to provoke considerable discussion in the lay and medical press. Although several small groups of cases have been reported, no comprehensive epidemiological study has been published. From the meager reports obtainable it is possible to divide these cases into two classes:

1. Uncommonly severe and frequent nasopharyngeal infections in adults, which in some few instances have been proved to be of influenza bacillus origin.

2. Infections in children, in whom gastro-intestinal symptoms have been so prominent as to divert attention entirely from the respiratory tract.

The general feeling has been that these infantile cases must in some way have been related to the adult type, and in consequence such a diagnosis as intestinal influenza has often been made; but not a single case reported has been substantiated by culture.

It is the group of infections in children with which this paper will deal. These are the cases in which the symptom-complex known as acidosis occurs and which have provoked so much discussion. Morse, in a recent article, has most ably reviewed the subject. He says in reference to the Boston epidemic: "It is my opinion that in the vast majority of instances the diagnosis of

acidosis had no reasonable justification. An epidemic of acidosis is impossible because of the etiology of the condition, and what has appeared to be an epidemic may be explained by the fact that a number of cases of secondary acid intoxication have happened to occur in the course of an epidemic of some other disease such as tonsillitis, la grippe, or nasopharyngeal infections." Holt states that 30 per cent. of 200 consecutive cases in the New York Babies' Hospital showed acetoneuria, and of all babies with pneumonia, 70 per cent. have acetone and diacetic acid in the urine. It is evident that so much attention has been paid to this peculiar group of symptoms that often no attempt has been made to determine the primary cause.

During the winter months there came to autopsy in this laboratory a small group of 3 cases which had shown the clinical picture of acidosis. All offered a common etiological factor and presented similar postmortem findings. Although the number of cases is too small to justify an attempt to draw from them any general conclusions regarding an epidemic of such proportions as the one just passed, yet this small series may prove of interest in connection with data which may be reported by others.

CASE I.—W. T., aged seven years. Complaint: difficult breathing; sore throat.

*Present Illness.* Sudden onset at midnight after feeling well previously; complained of sore throat, headache, and difficult breathing; became feverish and vomited. Sent by family physician to hospital, with a diagnosis of laryngeal diphtheria. Diagnosis by admitting physician: pneumonia.

*Physical Examination.* On admission the temperature was 103°. Pulse, 160. Respirations, 60. Patient dyspneic, cyanotic, and moribund. Heart sounds rapid and of poor quality; pulse small. Lungs: massive consolidation of right lower lobe, bronchial breathing, and coarse, moist rales throughout both lungs. Did not respond to stimulation, and died thirteen hours after onset.

*Autopsy* (15-144) one hour and ten minutes postmortem.

Body is that of a large, well-developed, well-nourished white male child.

*Larynx and Trachea.* These organs present on their mucosal surfaces considerable thick, viscid gray, purulent material. Microscopically the epithelium has disappeared and there is considerable superficial necrosis of the underlying tissues. Large masses of fibrin and a few pus cells have collected. In the surface necrotic material, in the folds of the mucosa and in the underlying tissue, are large masses of cocci.

*Pleural Cavities.* Left, negative; right contains approximately 300 c.c. of clear straw-colored fluid in which are small detached masses of fibrin. The visceral and parietal surfaces are covered with fresh fibrinopurulent exudate.



FIG. 1.—Tracheitis (15-141). Masses of cocci on surface; lining epithelium has undergone necrosis and disappeared; no membrane on surface; necrosis of underlying tissues below, which is an inflammatory exudate of polymorphonuclear leukocytes.  $\times 200$ . Gram-Weigert stain.



FIG. 2.—Portion of field in Fig. 1.  $\times 1000$ .

*Lungs.* Left, negative; right, the upper lobe and upper half of the middle lobe appears normal. The remainder of the lung is deep red in color, firm in consistence, and crepitation is entirely absent. This portion sinks in water. Section reveals a pale, purple-red surface with dark red mottling. On slight pressure considerable gray-green purulent material exudes from the bronchioles. Mucosal surface of bronchi covered with a similar material. Vessels appear normal.

The microscopic examination of the involved portion of the lung presents the following picture: Normal outlines are obscured by hemorrhage, which has distended and ruptured the alveolar walls. Its source is evident on examination of the vessels. Their lining endothelium is raised in places by accumulations of fibrin and endothelial leukocytes. Other vessels show an asymmetrical thickening of the intima which a scharlach R preparation demonstrates as due to an accumulation of fat in the intima. This injury in places is so severe that rupture has resulted. Occasional small deposits of fibrin occur immediately about the vessels. Lying in the large areas of blood-filled alveoli are great masses of cocci. The amount of purulent exudate is small. The bronchioles have also been invaded by hemorrhage; some contain small collections of leukocytes. The lung tissue immediately surrounding that involved by hemorrhage is edematous and is infiltrated with numerous polymorphonuclear leukocytes.

*Spleen.* Weight, 120 grams. The capsule is smooth and of a deep red color. Section reveals a firm, plane surface, dark red in color, on which the Malpighian corpuscles are readily visible as yellowish points. Trabeculae not prominent. Microscopically the vessels and sinuses are seen to be injected. The vessel walls present an asymmetrical, hyaline thickening, with partial occlusion of the lumen. Scharlach R demonstrates the presence of fat deposits in the intima just beneath the lining endothelium. The germinal centers are filled with fatty endothelial cells, which are incorporating and digesting lymphocytes. Some of these endothelial cells are in mitosis. No fat is present in unphagocyted lymphocytes nor in endothelial leukocytes not engaged in phagocytosis, nor is it present in endothelial leukocytes which have taken up blood pigment. Small fat droplets occur in polymorphonuclear leukocytes scattered throughout the pulp.

*Kidneys.* Combined weight 170 grams. Organs not remarkable in gross. Microscopically the only lesion demonstrable is an extensive deposit of fat in fine and coarse droplets in the epithelium of the convoluted tubules and in the loops of Henle.

*Adrenals.* Appear normal in gross. Microscopically the cells of the glomerulosa show a vacuolization of their cytoplasm due to increased lipid content. The nuclei are pyknotic. No leukocytic reaction is present. The fat cells in the tissue about the organ are of embryonic type.



*Lymph Nodes* (mesenteric and cervical). Enlarged, firm in consistence, and of a dark red color. On section they present a homogeneous pink-red surface. Microscopically they show marked endothelial hyperplasia and phagocytosis similar to that in the spleen.

*Gastro-intestinal Tract.* Stomach and jejunum not remarkable. Throughout the ileum the Peyer's patches and solitary follicles are markedly swollen and of a dull red color. The lymphoid tissue of the colon is likewise hyperplastic. Microscopically the intestinal lymphoid tissue resembles that of the rest of the body.

*Aorta.* Shows microscopically rather extensive fat deposits in the intima just beneath the endothelium.

*Thymus.* Weight 30 grams. Extends well over the anterior surface of the pericardium; appears normal.

*Blood* in all the organs shows a large amount of free fat demonstrable by scharlach R as globules lying free in the serum.

*Heart, Pancreas, Liver, and Genito-urinary Organs.* Negative. Cultures from the heart's blood, bronchial pus, and laryngeal exudate show *Staphylococcus pyogenes aureus* in pure state.

*Diagnoses.* Acute laryngitis and tracheitis; *Staphylococcus aureus* septicemia; lobular pneumonia with intense hemorrhage; toxic reactions in the lymphoid tissue of the body, in the arterial walls, in the renal epithelium, and in the glomerulosa of the adrenal; lipemia; embryonic type of cell in the body fat.

CASE II.—M. O'N., age less than one year.

A small, poorly-nourished white female child admitted to the contagious wards with aphonia, a croupy cough, stridor, and a slight serous discharge from both nares. Tonsils slightly enlarged, no membrane; slight posterior nasal discharge. Few small posterior cervical glands.

*Laryngoscopy.* Redness and congestion of rim; thin gray membrane covers entire larynx above cords and extends over rim anteriorly. Small piece of detached membrane hanging from right arytenoid. Patient intubed immediately and given 22,000 units of antitoxin. Temperature, 103°; pulse 150; respirations, 60.

On the third day after admission the temperature dropped to 99° and respiration to 42; pulse, 150. Patient suddenly became cyanotic, relaxed, and stopped breathing. Extubed and artificial respiration employed without success. Diagnosis: diphtheria. Cultures taken from nose and throat on admission negative for diphtheria bacillus.

*Autopsy* (15-147) eighteen hours postmortem.

The body is that of a well-developed, poorly-nourished white female child. The anatomical lesions are similar to those of Case I, including laryngitis, bronchopneumonia, and hyperplasia of the lymphoid tissues throughout the body. Microscopically the larynx shows a more extensive necrosis than Case I; the bronchopneumonia

is of the usual type and is unaccompanied by severe hemorrhage. The hyperplasia and phagocytosis with fatty changes in lymph nodules correspond exactly with the picture in Case I. The involvement of the renal epithelium and of the intima of the aorta are more severe, especially in the former location, where extensive fat deposits occur in all portions of the tubular epithelium. No changes in the adrenal are seen in this case. A lipemia of moderate degree is present, demonstrated as in Case I.

The bacteriological findings here cannot be given as much credence, as the cultures were taken eighteen hours postmortem. The absence of diphtheria bacilli in cultures taken at laryngoscopy is significant; no record was kept of the presence or absence of staphylococcus. Postmortem cultures showed *Staphylococcus aureus* in pure culture in the larynx and left lung, where it is also seen in sections. The right lung shows pneumococcus on culture.

CASE III.—M. Q., aged two years.

*Family and Past History.* Negative.

*Present Illness.* Six days ago nose began to discharge. Fever and cough; no convulsions or chills, vomited yesterday.

*Physical Examination.* Patient cyanosed; breathing rapidly; eyes glazed. Marked aphonia and stridor. Dulness over entire left back. Distant bronchial breathing. Many rales in both lungs. Laryngoscopic examination reveals marked swelling of the right arytenoid cartilage, redness, and swelling of the larynx and membrane on both cords. Smears show staphylococci.

*Autopsy* (16-33) eleven hours postmortem.

Body is that of a well-developed, well-nourished, white female child. The principal anatomical lesions are acute laryngitis, bronchopneumonia, acute exudative laryngitis, and general hyperplasia of lymphoid tissue.

Microscopically the reaction in the larynx is very extensive, comprising a phlegmonous inflammation of all structures down to and involving the perichondrium. The anatomical diagnoses of bronchopneumonic and acute exudative pleuritis are confirmed. The lymphoid reaction is similar to that in the previous cases. All portions of the renal epithelium show very extensive fat deposits.

Culture from the larynx obtained immediately after death through the laryngoscope showed staphylococcus in pure state. Further cultures at autopsy, eleven hours later, show a variety of organisms in the heart's blood and pneumococcus in the pleural cavity.

The striking features common to these cases may be briefly summarized as follows:

All are due to infection of the respiratory tract, with *Staphylococcus pyogenes aureus*. Case I shows in addition a septicemia.

All show an acute laryngitis, bronchopneumonia, and various toxic reactions appearing in lymphadenoid tissue, in the walls of

bloodvessels, in the renal epithelium, and in one instance in the adrenal cortex.

The severity of the lesions varies distinctly with the virulence of the infecting organisms, but in all the type of reaction is the same. Toxic reactions predominate to such an extent that in Case I, where a bacteremia is present, no abscesses occur in the viscera. Most unfortunately no urine analysis was made on any of the cases. From clinical evidence it is reasonable to suppose that acetonuria may have been present.

*Bacteriology.* The organism recovered from Case I has been most extensively studied and has been the strain employed in all experimental work. It was obtained in pure culture from the heart's blood, larynx, and lungs. No diphtheria bacilli could be found in smear or culture from the larynx. Culturally and morphologically this organism is a typical *Staphylococcus pyogenes aureus*. Its cultural characteristics may be briefly stated as follows:

On all ordinary media in twelve to eighteen hours there appear pale yellow discrete colonies which soon change to deep orange color and become confluent.

Litmus milk is coagulated, but no acid is produced in twenty-four hours; after forty-eight to seventy-two hours a very faint acidity is noted.

On Dunham's peptone indol is formed and nitrates are reduced. Gelatin is liquefied.

By Eijkman's method it was demonstrated that this strain of staphylococcus would produce a lipase *in vitro*, while two strains known to be non-pathogenic failed in this particular. His method in brief is as follows: A thin layer of sterile melted beef fat is poured in a Petri dish. This is allowed to harden and then a thin layer of agar at 42° C. is poured on its surface. Transplants are made in the usual manner on the surface of the agar. After twenty-four to seventy-two hours the fat underlying colonies of lipase-forming organisms becomes white, opaque, moist, brittle, and adherent to the underlying glass, due to the splitting of the fat and formation of fatty acids. Under colonies of organisms possessing no such power the fat remains unchanged.

On blood agar in twenty-four hours the colonies are surrounded by a zone of hemolysis. The following carbohydrates are fermented with the production of acid but no gas: dextrose, saccharose, mannite, raffinose, and maltose. No changes are produced in dextrin, salicin, and inulin.

*DISCUSSION OF LESIONS. Laryngitis.* There have been occasional references in the literature to the production of true diphtheritic membrane in the larynx by *Staphylococcus aureus*. Neisser states that he has seen "isolated cases with dense diphtheritic membrane (of such origin) which in one instance extended into the bronchi; postmortem bacteriological findings were definitely

established, no diphtheria bacilli being found but only *Staphylococcus aureus* in pure culture." In the records of this laboratory extending over a period of twenty years, however, not one case could be found in which a laryngitis was excited by uncomplicated staphylococcus. It is possible that, owing to the importance of diphtheria bacilli in this location, observers have failed to report the presence of staphylococcus, regarding it as a contamination or secondary invader.

In this present series all 3 cases present the picture of a very strong toxin acting locally to produce extensive necrosis of tissue. In Case I the body is reacting most vigorously with cellular exudation and the formation of fibrin in the deeper tissues. In Case III the invading organism seems to have the upper hand and only marked necrosis with little or no cellular exudation or fibrin deposit is seen. It is conceivable that had the toxin been allowed to act over a longer period of time true membrane might have been formed.

*Bronchopneumonia.* In all 3 cases this process is apparently due to direct extension from the larynx. The pulmonary involvement is comparable in all the cases, although Case I is complicated by marked toxic vascular lesions and embolic abscesses, and in the second case an acute exudative pleuritis accompanies the process.

Occasional reference to staphylococcus pneumonia is made in the literature, but its frequency appears to vary. Soper reports a series of 40 cases of all ages showing positive staphylococcus blood cultures, 30 per cent. of which developed pneumonia. Weichselbaum in a small series of 5 cases of pneumonia finds 20 per cent. due to staphylococcus. Dürk among 41 cases of pneumonia in children finds 50 per cent. due to *Staphylococcus aureus*. Schottmüller has recently reported a series of 4 cases of infection of the respiratory tract, which is almost parallel to those above described. His cases all occurred in young and healthy infants, with sudden onset, marked dyspnea, and cyanosis. All progressed to pneumonia and later empyema. Only 1 recovered; 3 came to autopsy. The latter showed uniform findings, namely: redness of the pharynx, exudate in the trachea, unilobular pneumonia, and empyema. In every case a pure culture of *Staphylococcus aureus* was recovered from all of the involved areas as well as from the heart's blood. No abscesses in remote viscera could be found. It is unfortunate that no histological examination of the trachea, lymph nodes, etc., was made, but it may be presumed that lesions were present.

The laboratory records of this institution show 860 cases of bronchopneumonia in individuals of all ages. Only 1.2 per cent. of this number are due to *Staphylococcus aureus* and less than 0.5 per cent. of the total number occur in children under the age of ten. In no instance has a sufficiently large number of cases been reported to allow of definite conclusions as to its frequency, and, moreover, it is likely that a staphylococcus is often disregarded as being a secondary invader.

*Toxic Reactions.* These lesions present the most interesting points for discussion and suggest many problems for experimental study. In general they resemble those encountered in the acute exanthemata, *e. g.*, diphtheria, scarlet fever, measles, and pertussis. In all of these conditions the respiratory tract is involved early in the course of the disease. In most of them the infecting organism remains localized and the changes throughout the body are due to the absorption and distribution of the toxin through the blood or lymph streams. The abundant lymphatic supply of the larynx seems especially favorable for such toxic dissemination.

The reaction in lymphoid tissue consists in active phagocytosis of lymphocytes by the endothelial cells lining the reticulum of the lymph nodules and a corresponding activity of the lymphoblasts (evidenced by frequent mitoses) to supply the deficiency of lymphocytes. The digestion of lymphocytes within endothelial cells is accompanied by considerable fat production, so that on examination of a seaharlach R preparation of the spleen, for example, the centers of the nodules appear at first glance to be a mass of fat. That the formation of fat results only from destruction of lymphocytes is apparent from the fact that neither the inactive endothelial cells nor the unphagocyted lymphocytes contain fat. Mallory interprets the reaction as a utilization of the lymphocytes for food by the endothelial cells which are producing antitoxins. As a possible alternative he states that lymphocytes injured by toxin may be taken up to be destroyed by endothelial cells.

This reaction in lymphoid tissue is constantly excited by the staphylococcus toxin. It has been noted in every instance of staphylococcus septicemia in the laboratory records, twenty-four in number. In addition to the above-mentioned exanthemata it is also common in the septicemias of children and adults due to pneumococcus and streptococcus and in epidemic cerebrospinal meningitis. Local reactions occur in the mesenteric lymph nodes during peritonitis and in the mediastinal and bronchial groups in pneumonias.

Injury to vessel walls apparently results from the direct action of the circulating toxin on the intima. This injury to the cells causes the production of varying amounts of fat which is taken up by phagocytic endothelial leukocytes. In the repair process more or less fibrin may collect beneath the endothelium. Such reactions are found in the aorta and in the smaller arteries of the spleen and lung. In the latter locations the injury has been so severe as to result in hemorrhage. In the spleen especially, large amounts of fat have collected in the intima to produce an asymmetrical thickening. Although such vascular reactions may result from the action of many bacterial toxins, that of the staphylococcus would seem to be especially active in producing these lesions. It is of interest to note in this connection that small, repeated intravenous

injections of staphylococcus have been used by Starkadowski, Saltykow and others in the production of experimental arteriosclerosis.

The lesions of the kidney are also of interest. All cases show fat deposits in various portions of the tubular epithelium, but there is neither apparent uniformity of distribution nor direct relation to the strength of the toxin. Similar changes occur in other acute infections, but examination of numerous kidneys from children dying from causes other than infectious fails to reveal any fat.

One instance of a disturbance in the normal lipid content of the cells of the glomerulosa of the adrenal occurs in this series.

The fat content of the circulating blood as seen in scarlach R stained sections is everywhere apparently increased, but no chemical determinations on the blood itself have been made.

These various metabolic disturbances, indicated by an increase of fat in the blood serum, by extensive pathological deposits in various organs, and by disturbances in the large deposits of fat tissues occurring throughout the body, opens an interesting field of speculation as to the origin of the acetone bodies in the urine. It has been demonstrated that the organism here studied produces a lipase on Eijkman's medium, and evidence of lipolytic action is everywhere present in the tissues. Although the presence of acetone bodies in the urine was not demonstrated in a single instance, yet it is reasonable to suppose that they were formed, as Hammarsten states: "At the present time the tendency is more and more to the view that the acetone bodies do not originate from the proteins but from the fats; if they are not the only source they are at least the most important." And to quote Howell: "Perhaps the most significant fact known bearing on this point (the oxidation of long carbon chain fats) is that under conditions which involve a large destruction of the fat in the body, as starvation, fevers, and especially diabetes, B. oxybutyric acid, together with aceto-acetic acid and acetone, is excreted in the urine." May not the action of this lipase in setting free fats in the circulation be a possible explanation for the presence of acetone bodies in the urine? Is not the frequency of acidosis in these children due to toxemias of various bacterial origins rather than to the fever, which is itself merely a symptom of intoxication? These and other questions present themselves, but they must be answered by the biological chemist.

**ANIMAL INOCULATION.** The reaction in the human body to this particular strain of staphylococcus was so manifestly toxic in character that an attempt has been made to reproduce these lesions in animals. The results have not been especially striking in that no single animal would present all the features common to the human cases, but, nevertheless, all the essential features have been reproduced in different animals.

A few preliminary inoculations with the freshly isolated organism

were made on guinea-pigs. These animals promptly died after twelve to twenty-four hours, without demonstrable lesion except in the case of intraperitoneal inoculation which showed considerable blood-tinged fluid.

Four months later this study was continued and a series of twenty-two young rabbits were inoculated in various ways. A small series of four animals was used to increase the virulence of the organism. Transfers were made from the subcutaneous tissue of one animal to another in rapid succession. The first animal lived four days, the second seven days, and the last two less than twenty-four hours. At the site of inoculation they showed an extreme degree of hemorrhagic edema. Toxic reactions in lymphadenoid tissue, renal epithelium, and the myocardium were parallel to those in the human cases and showed a quantitative increase proportional to the virulence of the organism.

Simple intravenous inoculation, although it killed two animals in twenty-four hours, produced no toxic reaction. Early abscesses developed in the heart and kidneys of both rabbits.

When intravenous inoculation was combined with pulmonary irritation (inhalation of ammonia or formic acid) three animals died in twelve to twenty-four hours, with marked edema and congestion of the lungs, and in one instance an early subpleural abscess. The lymphadenoid tissue in all these cases presented more or less toxic reaction. Fatty change in the renal epithelium and cardiac muscle was variable, being marked in two instances and absent in the other two.

In three animals intravenous inoculation and pulmonary irritation were combined with the action on the vagus of chloral hydrate given per rectum in dosage of 0.2 gram per kilo body weight. These animals developed no pulmonary lesions, but marked toxic reactions in lymphadenoid tissue occurred. The renal epithelium and cardiac muscle were involved to a moderate degree.

In two animals the left vagus was sectioned and ten minutes later a suspension of staphylococcus was injected through the cricothyroid membrane into the larynx. Both rabbits died in twenty-four hours, and at autopsy showed a purulent laryngitis; one had developed a lobar pneumonia involving both lobes on the side of the vagus section; the other showed an early pleurisy. Both presented more or less reaction in the lymphadenoid tissues, although not so marked as that following subcutaneous inoculation. The renal epithelium and myocardium had developed rather marked fatty changes.

In one instance deep intratracheal insufflation of a staphylococcus suspension was followed by a bronchitis which killed the animal in ten days. Mild toxic reaction occurred in the peribronchial lymph nodes.

An attempt was made to determine whether this organism produced a soluble toxin, for which purpose a modification of the

technic recommended by Neisser has been employed. The organism was grown for thirteen days at 37° C. on meat-sugar-free, 0.5 per cent. dextrose bouillon. At the end of this period the culture was centrifuged and the supernatant fluid was passed through a Berkefeld filter. Five per cent. of preservative composed of phenol 10, glycerin 20, and aq. dest. 20 was added.

The first rabbit of the series developed snuffles and was disregarded. The second animal received 7.75 c.c. of the filtrate in eight days. On the ninth day it was killed but no toxic lesions could be found. The third, which received a large dose (1 per cent. of body weight), died after fifteen days. The only demonstrable lesion was marked edema and congestion of the lungs.

Three animals were given intraperitoneal injections of this filtrate in doses of 6, 10 and 10 c.c. respectively. These died in from fifteen to forty-five days. Microscopically all presented focal collections of endothelial leukocytes in the liver. The spleens showed dilated sinuses in which the lining endothelial cells were actively phagocytizing erythrocytes. The kidneys in every case presented toxic reaction evidenced in the presence of hyaline droplets in the epithelium of the convoluted tubules.

The results of these experiments are in many respects disappointing, for in no single instance was it possible to reproduce the whole picture seen in human cases. It would seem that the greatest absorption of toxin in the rabbit takes place from the subcutaneous tissues rather than from the larynx. Toxic disturbances of fat metabolism undoubtedly have been reproduced in this animal, but they are not nearly so marked as those in the human being. The accidental findings when filtrates were injected into the peritoneum are of interest, but in no way represent changes produced in the human body.

**SUMMARY AND CONCLUSION.** Uncomplicated *Staphylococcus pyogenes aureus* is capable of infecting the upper human respiratory tract with the production of severe local lesions.

In these 3 cases the reaction on the part of the body is not of the type usually associated with this organism, *i. e.*, simple exudation in the immediate presence of the bacteria, but it rather resembles the general reactions seen in the acute exanthemata.

Remote reactions of this type are constant in all of these cases, and comprise changes characteristic of a severe toxemia. They occur in the lymphoid tissue, in renal epithelium, in arterial walls, and in the fatty tissues. Each of these lesions is associated with the production or formation of fat, and a large amount of fat is present as globules free in the blood serum. In addition the presence of a lipase formed *in vitro* by this strain of organisms has been demonstrated.

Although it cannot be proved by morphological study alone, it seems plausible to suppose that some direct relation exists between these disturbances of fat metabolism and acetonuria.



Whether this peculiarity of reaction is due to some inherent quality of this particular strain of staphylococcus or whether it is a result of the anatomical distribution of the organism is uncertain. That the former explanation is correct may be inferred from animal experimentation. In the rabbit it has been possible to reproduce remote toxic reactions by means of inoculation in several different tissues, most notably the subcutaneous tissues and the lungs indirectly through the blood stream with the aid of a local irritant and depression of the vagus.

These cases also illustrate the necessity for examination of the larynx, an organ often neglected by pathologists in the course of routine autopsies. This is especially important in children showing hyperplastic lymph nodes.

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### URINARY INFECTIONS OF PREGNANCY AND THE PUERPERIUM.\*

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THE pregnant or parturient woman presents problems that bring her within the purview of every practitioner and specialist in medicine and surgery. She is a specially interesting and important

\* Read before the Giles County Medical Society, Newport, Va.

patient, for upon the well-being of the mother depends also the safety of her coming or newborn child; hence two lives may be at stake whenever she becomes ill. And then, though pregnancy and the puerperium are physiological processes, they gravitate by such imperceptible degrees into the pathological, that to tell the normal from the abnormal is at times as difficult as to say when daylight ends and darkness begins. We are ever too apt to pass by complaints of the pregnant woman, regarding them only as inconveniences of her gravid state, until we are forced by explosive demonstration of symptoms to recognize the gravity of the situation.

It is with these considerations in mind that I present for your consideration the subject of infections of the upper urinary tract as a complication of pregnancy and the puerperium.

Neither pregnancy nor the puerperal state cause pyelitis nor any other of the urinary infections. On the other hand, both stand in the causal relation of predisposing to such infections. That is, the pregnant woman is only the more liable than the non-pregnant to such risks. Therefore we are at liberty to consider pyelitis in general, with only more particular reference to the aspects of the case introduced by the complication of actual or recent pregnancy.

The active or actual cause of urinary infections is the invasion of the urinary tract by pyogenic organisms. Nearly any organism may be responsible, but we have learned that one is much more frequent than the others. Every writer upon the subject lays stress upon the large percentage of colon bacillus infections. Of 23 patients of one series but 1 was produced by the streptococcus, and in all of the others the colon bacillus was the responsible agent.<sup>1</sup> When the infection, however, ascends from the bladder the streptococci and staphylococci are more apt to be present. A true gonococcus infection has scarcely ever been encountered in the higher portions of the urinary tract.

As just hinted, infections of the kidney and the pelvis of the kidney may arise through two channels: ascending from the bladder or through the lymph or blood channels. We must admit the possibility of infection of the higher urinary tract, ascending along the lumen of the ureter from the bladder; but experiment confirms the belief that lymph- or blood-borne infections are much more frequent.<sup>2</sup> And even in the not infrequent case in which the primary or secondary focus is the bladder the transmission of the infecting agent seems to be by way of the blood or lymph stream to the kidney rather than through the lumen of the ureter.

One of the interesting developments of modern medicine is the growing revelation of what we might call metastatic infections from remote and apparently innocuous foci. Urinary infection is no exception. In nearly every case some distant focus has antedated the urinary infection. In such connection, tonsillitis, otitis media, pyorrhea, cholecystitis, appendicitis, and salpingitis<sup>2 3 4</sup> have each

been indicted in the individual cases. But far above all other depots of supply for metastatic urinary infections is the intestine. The frequency of infection originating in the bowel accounts for the fact that the colon bacillus is oftenest the responsible organism. Infection of kidney from bowel without intermediate lesion has been a puzzling problem until recently Franke demonstrated an actual, direct connection through the lymphatics between the colon and the right kidney, which explains the preponderance of right pyelitis. These germs make their way from the cecum and colon through the posterior wall of the bowel and often also from the duodenum, without necessarily piercing the serous covering of the intestine. They pass readily to the lymph vessels in the kidneys and also into the ureters. The bacilli while in the bowel act usually as saprophytes, but when they are brought into contact with the urine they become pathogenic; while in the bowel they produce no antibodies; while in the urine they form spores.<sup>5</sup> As an interesting side-light on these colon bacillus infections from the bowel, "pediatrists have recently called attention to the comparative frequency of bacteriuria following extreme constipation, while the lower urinary passages remain persistently normal. Bumm has recently reported a significant case: intestinal trouble developed after excessive ingestion of milk and pyelitis followed, both promptly subsiding as the milk was discontinued."<sup>4</sup>

We must admit, too, that women, and especially pregnant women, are prone to these infections. The explanation of this susceptibility is not hard to find. Harttung<sup>6</sup> experimented by tying a ligature around a ureter in sixty-two rabbits. He found that the conditions thus induced invited suppurative changes in the kidney. When the infection was of ascending origin the kidney pelvis was involved first and predominantly, while with blood-borne infections the cortex suffered most. Couple this bit of experimental evidence with Weibel's<sup>7</sup> discovery that of one hundred normal pregnant women the ureters were more or less obstructed in 47 per cent., and predominantly on the right side, and we seem to have proved the problem. Ptoses, so common in women, and especially so in those who have been exposed to the drag of frequent child-bearing;<sup>8</sup> the pressure of the pregnant uterus upon adjacent organs, causing constipation and distention of the bowel with gas, so commonly observed in pregnancy; the dilatation and paresis of the pelvis of the kidney and ureter are favorable for the passage of the colon bacillus from the intestine; and the dilatation and paresis of the ureter and pelvis of the kidney assist in the infection of the urinary tract.<sup>5</sup>

In many cases pyelitis is present before pregnancy supervenes, and gestation but causes the process to become active.

"Acute infections of the kidney, primary in nature" (that is, so far as the urinary tract is concerned), "can be grouped anatomico-pathologically into three classes:

- "1. The pyelitic group—infection of the pelvis of the kidney alone.
- "2. The pyelonephritic group—infection of the pelvis plus infection of surrounding functioning portion.
- "3. The cortical group—infection of the cortex or functioning portion only."

Each of these groups give a distinct clinical and urinary picture, and to some extent the treatment is modified in each. From 60 to 80 per cent. will be included in the pyelitic group.<sup>9</sup>

The onset and course of this disease in its acute phases differ to a certain extent with the exact location or extent of the trouble, whether pyelitic or cortical especially. Within the recent past I have had opportunity to study 4 of them, 3 in pregnant women and 1 postpartum. The symptoms of the first 3 were singularly similar, and it will perhaps give a more practical turn to a discussion of the symptomatology if the case history of each of these be briefly abstracted:

1. White woman, aged twenty-nine years, complains of irregular chills for the past five days. She is six and a half months pregnant, the pregnancy so far being without complication. Since her first chill, five days ago, she has had two each day, followed by high fever, free sweating, and much aching. Aside from nausea she has had no other essential symptoms, no real pain except the general aching. She is seen just after a hard chill: pulse 163 and temperature 102°. She is apparently about seven months pregnant, the fetus in normal position. Marked tenderness is found in both flanks, especially over the left kidney posteriorly. The catheterized specimen of urine is loaded with pus. Leukoeytes only 5200 per c.mm.

2. White woman, aged twenty-three years, complains of pain in the right abdomen of three and a half days' duration. She is seven and a half months pregnant for the first time. Three and a half days ago she began vomiting and soon after was taken with severe right-sided adominal pain, requiring two or three hypodermics to relieve her. Pain and vomiting have continued intermittently since. Temperature has ranged between 100° and 102°. Upon examination there is found much tenderness over the lower right abdomen, over the appendix. There is also tenderness in the right costovertebral angle over the kidney. The catheterized specimen of urine contains great numbers of pus cells. Leukocytes 14,600 per c.mm., with a polymorphonuclear count of 80 per cent.

3. White woman, aged twenty-two years, complains of pain in the right abdomen of five days' duration. She is between five and six months pregnant for the first time. Since being taken with a sudden right-sided abdominal pain five days ago she has continued to have more or less intermittent, colicky pain, with fever very high, a rapid pulse, and tenderness over the appendix. At examination pulse is 132, temperature 101°; slight tenderness can be made out over the right flank, but nowhere else at this time. An examina-

tion of the catheterized specimen, without centrifugalization or sedimentation, showed only six or eight pus cells to the field and rare red blood cells. But two or three days later another specimen was simply loaded with pus. Leukocytes 13,000; polymorphonuclears, 82 per cent.

Constructing the symptomatology then upon these cases and the recorded experience of others we might say that usually the woman has run the normal course of pregnancy until at some time during the second half she suddenly develops a chill, followed by high fever, sweating, then an intermission or remission of temperature. Or instead of a positive chill there may be only a sense of chilliness or of rigors, with fever marked by great irregularity. Sometimes pain is the more marked symptom, and with the pain vomiting and tenderness in the abdomen. The pulse is usually higher than the temperature would justify. As a rule, however, with the simple pyclitic group, the woman does not look as sick as one would expect.

Upon examination one expects to find on deep pressure over one or the other kidney some tenderness. One of our cases gave no tenderness anywhere, in spite of the fact that her urine contained quantities of pus.

The most interesting case of all perhaps was the one developing only after some weeks postpartum:

4. White woman, aged twenty-three years, complains of irregular fever and chills for the past eight days. Her first baby was born four and a half weeks ago, after a normal labor, being delivered by an obstetric specialist whose hands were protected by rubber gloves. Two days after delivery the patient was found running fever. Her physician made out what he considered was a valvular murmur and immediately suspected acute endocarditis, originating, he thinks, from thrombosis in a uterine sinus. From this time on she continued to run a little irregular fever, and developed an increasing degree of anemia, though she has been allowed to get up and about her room. Two weeks ago, the fever continuing and the other evidences of sepsis becoming more marked, a consultant advised puncture of the posterior cul-de-sac, suspecting pelvic pus. Another physician examined her pelvis at this time and could find nothing abnormal there. At this time her leukocytes were 14,000. Eight days ago the patient's temperature suddenly shot up much higher than it had ever been before, and then swung a distinct septic curve, between  $99^{\circ}$  and  $104^{\circ}$ , pulse 80 to 120. Her urine has been examined chemically only and pronounced negative. A third consultant has seen the patient, and, finding a murmur about the heart, has pronounced the case one of acute (septic) endocarditis.

At the time of this consultation she is just over a hard chill and shows some exhaustion. Pulse 140, temperature  $103^{\circ}$ . She looks quite anemic and weak. A bruit is made out, not over the heart, but at the second left interspace, and only when the patient is lying

down. It is not regarded as valvular at all by this consultant, but as a so-called "hemic murmur." Pelvis and abdomen seem absolutely negative. There is no special tenderness in the flanks. The catheterized, but non-centrifugalized, urine shows only three pus cells and an occasional red blood cell to each field. Her leukocytes are 11,400; the hemoglobin was 75 per cent.

This seemed to the other consultants in the case too small an amount of pus upon which to make a diagnosis, but with treatment directed to this condition alone the patient had only one slight chill subsequently and went on to perfect recovery.

The interesting point came out afterward that the patient throughout her later pregnancy had run a little irregular fever, which made her husband, a physician, fear tuberculosis. The probability is that she had had pyelitis all of this time, but the symptoms only became stormy after delivery.

So the laboratory may be of inestimable help in the diagnosis or it may give a very confusing negative report. As a rule, and as would be expected, there is more or less leukocytosis, with the polymorphonuclear elements predominating.

If one can only remember to think of examining the urine of all pregnant women, in the great majority there should be no trouble in recognizing urinary infection when it exists. Of course it is manifest that the specimen must be catheterized into a clean vessel. Even without the microscope one can be fairly certain of the condition from the gross appearance of the urine. If it be held against the light in a clean glass vessel, and it is seen to be turbid, and especially if ragged shreds of purulent appearance float around in the urine, the changes are strong that a urinary infection is present.

The microscope, of course, must be resorted to to make the diagnosis final. Too often the physician examines the urine for albumin, finds it present, and thinks of the case from that point on as one of nephritis, with the consequent purging and dieting which is not proper unless there be a certain element of nephritis complicating the infection. We need the microscope to differentiate between pus and casts as the cause of the albuminuria. Or, even more frequently, one will be surprised to find only a faint trace of albumin, with numbers of pus cells: if he is not in the habit of making microscopic urinalyses he will pass by such cases. With the pus there are usually numerous microorganisms, oftenest a motile bacillus, one of the bacillus coli group.

Of course there are many variations from this picture. One of our patients, with severe rigors and temperature of  $104^{\circ}$ , had only three pus cells to each field. It is easy to overlook such cases, most important of all, for in them the cortical portion of the kidney, its functioning part, is involved, and until the pus makes its way to the renal pelvis, where it can pass out through the ureter, we may not find a single cell, and the patient is all the sicker. The entire

kidney may be literally filled with minute abscesses, and yet not a single cell show in the urine. In another case there is a great deal more albumin, with far less pus, than in another with less albumin: in such cases we suspect a pyelonephritis and the microscope ought to show both pus and casts.

As one may easily guess, the diagnosis of these infections of pregnancy depends in large measure upon whether they are thought of as among the possibilities of the illness. "The important factor in its recognition is to remember that in the presence of the foregoing symptoms it is the most likely condition to be found as a complication of pregnancy."<sup>2</sup> The main "lead" in the greatest number is the toxemia. Toxemia, with high fever, chills, leukocytosis, and pus in an acid urine, with the presence of the colon bacillus in pure culture, should, of course, suggest the diagnosis. When pain is the prominent symptom the confusion that arises will depend upon how exactly it imitates some other pain. For instance, pleurisy may be suggested. The inflamed kidney moves painfully with breathing, suggesting at once a respiratory disease. In two reported cases pyelitis was actually accompanied by involvement of the pleura, the infection probably spreading through the lymphatics to the peritoneal and pleural sides of the diaphragm.<sup>3</sup> Pressure on the inflamed right ureter will often produce pain in the ileocecal region similar to that of appendicitis. It is peculiarly liable to be confused with appendicitis in those cases in which there is no change in the urine for the time being, or if the urinary changes are slight and transient, or if the ureter is blocked, so that only urine from the sound kidney is obtained by the catheter. Pyelitis may induce symptoms suggesting peritonitis: one case is reported in which laparotomy was done on the assumption of ileus from compression of the intestine by the gravid uterus.<sup>3</sup> Pyelitis may also simulate salpingitis, or puerperal infection. One case is mentioned in which the signs and symptoms suggested pneumonia, puerperal fever, appendicitis, and pyelitis all at once; but the diagnosis finally narrowed down to pyelitis alone.<sup>3</sup> In 2 cases profuse hematuria, for which the pyelitis was responsible, simulated uterine hemorrhages; it came on in 1 case like the hemorrhage of placenta previa.<sup>3</sup>

Practically, however, the greatest difficulty in the differential diagnosis is to distinguish these cases from acute appendicitis. We all recognize the fact that acute appendicitis is the most dangerous infectious complication to which a woman in late pregnancy is liable. To delay prompt operation may be fatal. We are aware of the fact, too, that some acute cases of appendicitis may show a little pus in the urine, and that a little pus may be all we expect in the acute renal case. No cut-and-dried differentiation will hold in every case. It has always struck me, however, that the chills, septic oscillations in the temperature, and the pain are more violent in the renal case than in the early appendicular one. One rarely requires

two or three hypodermics of morphin, for instance, to relieve the pain of early acute appendicitis; and seldom finds a chill with rise of temperature to  $103^{\circ}$ , with profuse sweating following, in the early days of an appendicular illness. These, coupled with pus cells in the urine, be they few or many, with the colon bacillus, and tenderness high up over the costovertebral angle, usually suffice to make the differentiation favor the renal source of infection.

The assumption that pyelitis of pregnancy does not require special treatment is wrong. I am sure that a number of mild cases never give urgent symptoms and are finally relieved after delivery more or less spontaneously. But when there are any real symptoms there is always danger for both mother and child. Opitz found that 40 per cent. came to premature delivery.<sup>10</sup> Another serious danger is the liability to breed puerperal infection. The woman comes up to labor, the placental site becomes infected through the blood stream, with consequent puerperal sepsis. As with eclampsia, there is reason to believe that there is more danger in pyelonephritis developing after delivery.<sup>11</sup> And they may be particularly hard to recognize. Murray,<sup>12</sup> for instance, reporting 8 cases commencing after labor, says that in 3 there was total absence of local signs and symptoms, temperature was remittent rather than intermittent, chills were absent, there were smaller amounts of pus in the urine, although the patients were seriously ill. The disease began on the day after delivery. He lost 1 out of the 8.

Like in many other conditions the ideal treatment of renal infections, whether combined with pregnancy or not, is impracticable for the general practitioner in the field in which he has to practice. It is not possible to gainsay the statement that the direct local treatment of the suppurative focus in the pelvis of the kidney and surrounding tissues through the cystoscope and ureteral catheter is the method of choice, theoretically speaking.<sup>2 4 10 11 17</sup> But fortunately we are not confined to this direct method of treatment, and have practical and for the most part efficacious modes of reaching the trouble, which can be carried out in the patient's home.

There is one rather mechanical mode of treatment that is probably not so often used as it deserves, that is, the distention of the bladder to its physiological capacity, the patient reclining with only the head above the plane of the bed. This reduces congestion in the renal pelvis, stimulates kidney secretion, modifies the urine, and thus combats the cause of retention and helps in the evacuation of the kidneys.<sup>11</sup> Posner<sup>4</sup> has encountered cases of pyelitis which dragged on for weeks or months and kept constantly recurring, and which healed promptly under daily rinsing out of the bladder with weak silver nitrate solutions in addition to the usual measures. He says that while the pyelitis may start from metastatic infection from the intestine, middle ear, or other infectious process it is kept alight by the secondary infection of the bladder and the muscular insuffi-



iciency on the part of the ureters. The stretching of the bladder in the local treatment may by reflex action arouse the kidney pelvis to contract and thus expel its contents better.

The drug treatment of urinary infections will be successful or the reverse in proportion to the rationality of the use of urinary antiseptics. Though in some degree foreign to the narrow title of this paper it may not be amiss to comment on the use and abuse of a certain drug which is thought of most prominently nowadays as soon as the word urinary antiseptic is mentioned. Hexamethylenamin is more often used indiscriminately and illogically than wisely. Any number of experimental and clinical observations could be cited, were it not a matter of common knowledge, that, to paraphrase Hinman,<sup>13</sup> hexamethylenamin, and all allied compounds, has absolutely no antiseptic value except as it is converted into formaldehyde, and except as the formaldehyde comes into contact with the infection. It is a further fact that formaldehyde cannot under ordinary circumstances be split off from hexamethylenamin unless the urine is acid. In fact, the percentage concentration of the formaldehyde in urine will depend upon the degree of acidity more than any other factor, which acidity should be greater than 2 c.c. of tenth-normal sodium hydroxide to 10 c.c. of urine. We know that we can increase the acidity of urine by feeding such drugs as the acid sodium phosphate,\* but even under ideal conditions hexamethylenamin at the level of the kidneys has no antiseptic value, in the usual dose, perhaps because of the rapid passage of the urine through these structures.<sup>15</sup> Further still, while formaldehyde is present in the bladder when hexamethylenamin is given in the ordinary dose, it is usually too small a quantity for any antiseptic value, and is usually voided too quickly for the time factor necessary for its disinfecting qualities to assert themselves.

These conclusions probably account for many of our failures with this drug. My own experience is that urotropin has rarely been of service in the upper urinary infections, perhaps because of the impracticability of getting the urine acid enough to split off formaldehyde during the rapid transit through the kidneys and ureters.

But when the infecting agent is the colon bacillus, the one method of treatment which has given me most satisfaction is alkalization of the urine, and the best drug for this purpose is potassium citrate. The plan is to give potassium citrate in sufficient dosage and with sufficient frequency to render the urine alkaline and to keep it so, day and night, for at least a week or ten days after all symptoms have disappeared. It will doubtless seem like an excess of

\* Jordan<sup>14</sup> offers the practical suggestion that whenever acid sodium phosphate is prescribed—and it ought always to be prescribed whenever urotropin is—one should write the chemical formula ( $\text{NaH}_2\text{PO}_4$ ) on the prescription, and to ascertain which phosphate has been dispensed. It is worth while, too, to occasionally test the urine to learn whether acidity is rising.

enthusiasm to say that one can confidently expect a rapid deferescence and a general improvement in all the other toxic manifestations within two or three days if this treatment is carried out intensively.

Yet one will be surprised at the dose of the citrate required to fulfil these conditions; 15 to 20 grains every two hours, and every three or four hours at night, will probably be the least that will accomplish it. A grievous disappointment is in store for one if the treatment be discontinued as soon as the symptoms abate.

As enthusiastic as I am about the effects of alkalization as emergency therapy, as it were, I must confess that I have found the ideal, *i. e.*, the disappearance of pus from the urine, exceedingly difficult to attain under this simple treatment. This has been specially true when it complicates pregnancy. The mechanical difficulty of proper drainage is doubtless responsible. At any rate if the microscopic appearance of the urine be followed from day to day one will note a great diminution in the total number of pus cells coincident with the clearing up of the acute symptoms about the second or third day. But after a sudden drop in the number the pus persists, however actively the citrate treatment be pushed. Paradoxically, I have several times had the report that the patient seems perfectly well and is rebelling at continuing treatment, and found the urine still full of pus. The explanation of improvement, with the infection still persistent, is most difficult. At any rate we cannot afford to stop treatment merely because the patient feels well.

In this dilemma I have had recourse to the newer vaccines: the "sensitized," or serobaeterins, the advantage of which is that carrying, as they do, their own antibodies the reaction is nothing like so probable nor so violent as with the older vaccines, and we can give ascending doses every day or every other day instead of at intervals of from three to seven days.

But while the stock vaccine has the advantages of being readily available and of offering its own antitoxins, practically, within its own substance, all stock vaccines are more or less of hit-or-miss prescriptions. This seems specially true of the colon bacillus. This organism alters its characters with its environment, and it is usually one of the many atypical varieties of the colon bacillus which causes these urinary infections. It is certain that the autogenous vaccines are much more efficacious.<sup>16</sup> As a rule improvement is rapid, and after the first dose the temperature may fall and the toxic symptoms be relieved, while the bacteria may disappear from the urine. But even so one must be guarded in giving a prognosis of rapid return to health or in discontinuing treatment too soon; for, though it may be easy to control the bacterial activity in some cases it is difficult and occasionally impossible to completely inhibit them. This treatment, too, should be controlled by periodical examinations of the urine.

Practically all reports are of the same tenor. Wulff,<sup>1</sup> for instance, reports after close study of 46 patients, 4 of whom were pregnant, and in all of whom the autogenous vaccines were used. The acute febrile attack was promptly arrested at one stroke and the tendency to recurrence cured. The rationale, as he explains, is similar to that of all vaccine therapy: the vaccine has put an end to the trouble either by destroying the primary focus or by modifying the system in some way, and in such a way that it is able to resist bacterial invasion. This latter seems to us the more likely because, as his experience indicates, that while 91 per cent of his cases were cured or materially improved under vaccine treatment the proportion of those who showed albuminuria was reduced only from 76 per cent. to 28 per cent.; of those who had pyuria, the reduction was from 100 to 41 per cent., but of those with bacteriuria the drop was from 100 only to 71 per cent. In other words, the infecting agents seem to be still present while the patient seems clinically perfectly well.

This conforms to common experience. Most of these pregnant women will continue to show pus in the urine, whatever the method of treatment, until they are confined, and yet under the vaccine treatment it seems to do them no harm, either during the further course of pregnancy, at labor, or during the puerperal period. The explanation is, probably, that the vaccine has conferred an immunity, though it is not able to overcome the mechanical obstacles to drainage, which are removed only by delivery.

To focus attention upon such points as may be of practical importance, one is justified probably in drawing the following conclusions:

1. Urinary infection as a complication of obstetrical practice is probably not rare. Just how frequent it is cannot be accurately stated. We have seen four cases during a period of time in which we have seen only one case of eclampsia.

2. Pregnant women are predisposed to urinary infection by reason of interference with drainage and by the further fact that conditions are ideal for transmission of infection.

3. The colon bacillus gaining entrance from the bowel is the usual infecting agent.

4. When a pregnant or puerperal woman has any febrile illness, whatever may be the type of fever, or whatever the associated symptoms, a catheterized specimen of urine should be obtained at the first visit. If this urine be cloudy, acid, and albuminous one should immediately suspect infection of the higher urinary tract and should make a microscopic examination before any other diagnosis is accepted.

5. Clinical signs and symptoms may be most confusing without, or even with, laboratory aid, and especially are we apt to miscall the case appendicitis, because the pain, tenderness, and rigidity are most often right-sided. In such case the right kidney region ought always to be examined for tenderness, etc.

6. Treatment which has been efficacious and at the same time practicable is (1) rapid alkalization of the urine with potassium citrate. This has been more certain, by far, than hexamethylenamin. Certainly, potassium citrate and hexamethylenamin should not be given at the same time, for one tends to render the urine alkaline and the other depends upon a high degree of acidity for any possible value; (2) in the meantime we can usually get a supply of the "sensitized" vaccine, of the colon bacillus, because it can be sooner given than (3) an autogenous vaccine, which should be prepared as soon as possible. Under such treatment all of our cases so far have been controlled until delivery has cleared up the picture. But should the symptoms persist stormily in spite of us, then the patient should be referred for irrigation of the kidney pelvis, or possibly even nephrotomy or nephrectomy.

7. Mere persistence of pyuria, on the other hand, we might say is to be expected, and need occasion no undue alarm, if the patient be symptomless, and especially if there be no fever at all and no leukocytosis. Such patients usually go to full term, with normal labor and puerperium, immune apparently from risks of their infection.

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## A SIMPLE PROCEDURE FOR PREPARATION OF COLLOIDAL GOLD FOR DIAGNOSTIC PURPOSES.

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THE first attempts to prepare colloidal gold in St. Luke's laboratory were made according to the procedure recommended by Miller, Brush, Hammers, and Felton,<sup>1</sup> but in spite of the greatest care the solutions obtained were uniformly poor. Eventually it was decided to experiment independently with a view of getting some insight into the trouble which we and many of our predecessors had experienced, and ultimately a reliable and exceedingly simple technic was evolved for preparing colloidal gold which will satisfy every clinical requirement.

The glassware used was the Pyrex brand. It was cleaned, with no more attention than that usually given to laboratory apparatus, and was rinsed only with tap water. Indeed, it was noticeable that solutions with which it came in contact did not wet the surface but tended to form in drops. It is advisable, however, to avoid beakers that have had bad scratches, as reduction tends to take place there.

Ordinary distilled water was used; no attention was paid to the time that elapsed since distillation, and it was drawn from stock containers. In view of the impurities possibly contained in some of the reagents<sup>2</sup> and the known toleration of colloidal gold solutions for electrolytes,<sup>3</sup> it is felt that in an emergency tap water could be employed, and satisfactory solutions have been made with it. All the reagents were obtained from Merck & Co. The potassium carbonate and oxalic acid were of the "Blue Label Reagent" quality,

<sup>1</sup> A Further Study of the Diagnostic Value of the Colloidal Gold Reaction, together with a Method for the Preparation of the Reagent, Bull. Johns Hopkins Hosp., 1915, xxvi, 298.

<sup>2</sup> The formaldehyde always contains formic acid. Ten c.c. of the formalin used required 1.1 c.c. of  $\frac{1}{10}$  NaOH for neutralization (phenolphthalein). The maximum limits of foreign substances in Merck's "Blue Label Reagent Potassium Carbonate" used were stated to be:

Heavy metals . . . . .	0.0000	per cent.
Chlorides (Cl) . . . . .	0.0020	"
Sulphates (So <sub>3</sub> ) . . . . .	0.0075	"
Nitrates (N <sub>2</sub> O <sub>5</sub> ) . . . . .	0.0800	"
Potassium cyanide (CN) . . . . .	0.0480	"
Sulphides (S) . . . . .	0.0200	"
Sulphites (SO <sub>2</sub> ) . . . . .	0.0080	"
Thiosulphates (K <sub>2</sub> S <sub>2</sub> O <sub>3</sub> ) . . . . .	0.0800	"
Phosphates (P <sub>2</sub> O <sub>5</sub> ) . . . . .	0.0040	"
Silicates . . . . .	0.0000	"
Aluminum (Al) . . . . .	0.0400	"
Calcium (Ca) . . . . .	0.0010	"

<sup>3</sup> 1.7 c.c. of 1 per cent. NaCl is necessary to precipitate completely 5 c.c. of colloidal gold in one hour. Five c.c. of colloidal gold will remain unaffected by 1 c.c. of 0.4 per cent. NaCl for an indefinite period.

the formalin U. S. P.; but there would seem to be no objection to using any good grade of chemicals convenient. The gold chloride was in sealed ampoules, and it is noteworthy that the weight of "gold chlorides" contained therein varies very considerably.<sup>4</sup>

The solutions were of the following strengths:

Gold chloride acid . . . . .	1 per cent.
Potassium carbonate . . . . .	2 "
Oxalic acid . . . . .	1 "
Formaldehyde (37 per cent. $\text{CH}_2\text{O}$ ) 2.5 per cent (5 c.c. formalin made up with 200 c.c.).	

The solutions should preferably be freshly made, although all but the last keep very well. The oxalic acid probably does not deteriorate at all, but the potassium carbonate slowly tends to dissolve its container and incorporate silicates; the gold chloride is easily reduced upon exposure to dust or light, and the formaldehyde undergoes marked changes from oxidation, polymerization, etc.

It was assumed that since good solutions had been prepared with 10 c.c. of 1 per cent.  $\text{AuCl}_3$  per liter, that that amount might not be considered excessive, provided that reduction was not carried too far. Keeping this constant, it was found that an increase of potassium carbonate tended to give violet and purple solutions. This was the experience of Miller, Brush, Hammers and Felton, and so the original amount of 7 c.c. was retained. These solutions, however, were invariably cloudy and more or less opaque. (Ten drops (0.43 to 0.58 c.c.) of oxalic acid and not more than 5 c.c. of formaldehyde were used.) The amount of oxalic acid was then gradually increased and a marked improvement was at once apparent. The solutions were very much more transparent and the minimum amount necessary to obtain the maximum transparency seemed to be about 1.75 c.c. This was also in accordance with the results obtained at Johns Hopkins, but the statement that "a large amount of oxalic acid without the subsequent addition of formaldehyde made clear 'satt rot' colloidal gold solutions" could not be verified. The solutions obtained in this laboratory were beautifully clear, but always blue or purple, although the conditions were varied within wide limits.

Finally, the formaldehyde factor was studied. It was evident from the behavior of the oxalic acid not only that the formaldehyde was essential to secure the ruby red color, but that it was responsible for the brown turbidity.<sup>5</sup> Beginning, then, with 5 c.c. the amount

<sup>4</sup> The contents of two tubes labeled as containing 15 grs (972 mgs.) of "Gold Chlorid Merck Acid" contained respectively 824 and 869 mgs.

<sup>5</sup> It is suggested that the brownish turbidity is caused by a suspension of reduced gold of almost molecular dimensions. Solutions which are fogged invariably deposit a brown precipitate transmitting violet light and resembling purple of Cassius and the violet gold precipitated from colloidal gold solutions by electrolytes. Such particles may have been caused by reduction by trioxymethylene (paraformaldehyde), and we have observed that when the Ostwald pipette used in measuring the formaldehyde is allowed to remain on the desk several hours, an amorphous white precipitate can be seen in the tip, and if the pipette is used a very cloudy solution results, whereas a clean dry pipette gives clear solutions.

was slowly reduced (1.75 c.c. of oxalic acid being used), and although for a long time no change could be noted in the appearance of the solutions, this very fact was proof that too much formaldehyde was being employed. Very suddenly, though, almost ideal solutions resulted, which, moreover, responded perfectly to known paretic spinal fluids. Flesch notes that he could not obtain good solutions unless he used much less than 10 c.c. of 1 per cent. formalin, usually 2 or 3 c.c.<sup>6</sup> The proper amount seems to be about 0.83 c.c. of 2.5 per cent., formalin containing 37 per cent., by weight of  $\text{CH}_2\text{O}$ , or 8.07 mg. of  $\text{CH}_2\text{O}$  per liter of colloidal gold made up.

In order, then, that the correct amount of formaldehyde should be used it is necessary to determine the value of the formalin. This may be conveniently done by a modification of the iodometric method of Ronijn,<sup>7</sup> which we have worked out as follows:

**EVALUATION OF FORMALIN.** Ten cubic centimeters of the formalin is made up to 1 liter with distilled water and 5 c.c. of this solution is mixed with 25 c.c. of decinormal iodine. Two normal sodium hydroxide is added drop by drop until the liquid becomes clear yellow. After ten minutes 2 c.c. of concentrated hydrochloric acid are added and the free iodine titrated with decinormal sodium thiosulphate. Two atoms of iodine are equivalent to one molecule of formaldehyde. If  $T$  equals the titration and  $S$  the specific gravity of the formalin, then

$$\text{Percentage of } \text{CH}_2\text{O} = \frac{75 - 3T}{S}$$

Up to this point the gold and alkali had been added at 60°, the oxalic acid at 80°, and the formaldehyde at 90°. The experiment was made of introducing all the chemicals initially, keeping the temperature just high enough to cause gradual reduction. The results were eminently satisfactory, and we have since been guided entirely by the color changes rather than by any definite temperature. This preliminary mixing of all the units of the reacting system insures their perfect and uniform distribution and eliminates the unfortunate and unavoidable local reduction effect entailed by the serial method of introduction of the reducing agents.

The following procedure has been finally adopted, and although it is not guaranteed to be infallible in giving ideal solutions; with a little experience it will be found not at all difficult to get 90 per cent. of the trials to answer every clinical requirement. As the cost of the chemicals is less than five cents per liter, and a dozen solutions may be prepared in an afternoon, it is no extravagance to discard even 50 per cent. of these should this be necessary.

**TECHNIC OF SECURING ONE LITER OF "SAT T ROT" COLLOIDAL GOLD.** To 1 liter of distilled water in a clean flask add 10 c.c.

<sup>6</sup> Flesch: *Ztschr. f. d. ges. Neurol. u. Psychiat.*, 1914, xxvi, 318.

<sup>7</sup> *Ztschr. Anal. Chem.*, 1897, xxxvi, 18.

of 1 per cent. gold chloride, 7 c.c. of 2 per cent. potassium carbonate, 1.75 c.c. of 1 per cent. oxalic acid, and 0.83 c.c. of 1 to 40 formalin (37 per cent.  $\text{CH}_2\text{O}$ ) or equivalent amount of 8.07 mg. of  $\text{CH}_2\text{O}$  per liter. Mix thoroughly, cover with a watch-glass, turn the burner on full and heat with occasional stirring to between  $80^\circ$  and  $85^\circ$ . Then reduce the flame enough to keep the temperature constant. The wire gauze supporting the beaker should be covered with a sheet of asbestos cardboard to prevent local reduction on that portion of the beaker directly over the flame. The solution will slowly develop through a series of colors substantially as given below, though some of the shades are much more transient than others. The associated temperatures are merely typical and were recorded for a development which lasted about an hour.<sup>8</sup>

When the solution reaches its maximum depth of color a remarkable lightening and change of color occurs within the space of a few seconds, and *until this rebound and transition of color has taken place the solution will be worthless for clinical purposes*. After this point has been passed, the burner may be turned out and the solution allowed to cool to room temperature, although if wanted at once there is no objection to cooling in running water.

If a solution is heavily eluded, pour it out and examine the flask for spots and streaks of reduced gold transmitting green, blue or violet light. If noticeably present, add a little aqua regia,<sup>9</sup> cover with a watch-glass and warm for a few minutes. Then rinse thoroughly and repeat the experiment. A clear colloidal gold solution leaves a clean container.

If the solutions still continue to be turbid and show a strong brownish fluorescence a series of 6 liters should be made with amounts of formaldehyde, decreasing and increasing by 0.05 e.e. from that originally used, and notice taken in which direction

<sup>8</sup> Kaplan observed that the color change comes gradually as a rule in good colloidal gold solutions: *Ztschr. f. d. ges. Neurol. u. Psychiat.*, 1915, xxvii, 246.

Color.	Temperature.
Faint blue green . . . . .	$65^\circ$
Pale blue green . . . . .	$74^\circ$
Pale bluish lavender . . . . .	$78^\circ$
Bluish lavender . . . . .	$79^\circ$
Pinkish lavender . . . . .	$80^\circ$
Bluish pink . . . . .	$82^\circ$
Pale pink . . . . .	$83^\circ$
Pink . . . . .	$84^\circ$
Deep pink . . . . .	$84^\circ$
Violet red . . . . .	$84^\circ$
Bluish red . . . . .	$83^\circ$
Deep bluish red . . . . .	$83^\circ$
Deep ruby red . . . . .	$83^\circ$
Dark ruby red (violet red in test-tube or pipette) . . . . .	$83^\circ$
Rebound or color transition . . . . .	$83^\circ$
Orange red (orange pink in test-tube or pipette) . . . . .	$83^\circ$

<sup>9</sup> Seven volumes of concentrated hydrochloric acid in two volumes of concentrated nitric acid.



improvement occurs. We have observed that too little formaldehyde will cause cloudiness as well as too much.

It is perhaps advisable to keep the solution in the dark, but it is not necessary to keep it cold, and so far as we know the solution once made will keep indefinitely, certainly for several months. Contrary to the generally accepted requirement a slight brownish surface-dispersion was found to make no difference in the practical application of the colloidal gold. The practice of Kafka<sup>10</sup> of rejecting all solutions which are tinged blue may be adopted, and it may also be stated for the guidance of those making colloidal gold that the correct color is duplicated almost exactly (in a test-tube comparison) by a solution of 5 c.c. of 20 per cent. by weight of cobaltous nitrate ( $\text{Co}(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$ ) plus 0.3 c.c. of 0.25 per cent., potassium bichromate ( $\text{K}_2\text{Cr}_2\text{O}_7$ ) solution, plus 10 c.c. of water.<sup>11</sup>

A certain amount of black sediment often accumulates on the bottom of the colloidal gold solution, but this does not impair its usefulness.

The procedure given above applies to the preparation of 1 liter of colloidal gold at a time, and it is not advisable to experiment with quantities greater or less than that amount until some experience has been gained.

None of the solutions prepared by this method were of the protected type, and all of them gave typical curves not only with general paresis but with lues, tabes, and meningitis. No attention was paid to the question as to whether the final solution was neutral or not, but 5 c.c. of every solution prepared was completely precipitated in one hour by 1.7 c.c. of 1 per cent. sodium chloride, and no change of color whatever could be detected with normal spinal fluids.

In an article by H. S. Hulbert<sup>12</sup> the inherent disadvantages of formalin are discussed and a neat method is shown of avoiding these by utilizing formaldehyde vapor, oxalic acid being omitted, and the course of the reaction being guided by the color of the solution.

The tubes used for the clinical tests were heavy glass, lipless test-tubes, measuring  $\frac{1}{6}$  in. to  $\frac{3}{4}$  in. x 6 in. They are not readily broken in washing, and the point of the 1 c.c. pipette may safely be pressed against the bottom of the tube in order to avoid air bubbles and danger of spinal fluid being carried into the mouth of the operator. After using they are rinsed in tap water and immersed overnight in a 1 to 10 dilution of aqua regia. This effectually dissolves any precipitated gold which may be sticking to the glass, and which it is difficult otherwise to remove.

<sup>10</sup> Kafka: *Deutsch. med. Wchnschr.*, 1913, xxxix, 1874.

<sup>11</sup> It is the intention to publish later the composition of a complete permanent standard colloidal gold color scale blended from inorganic constituents similar to the above, and based upon the colors observed with pathological spinal fluids.

<sup>12</sup> Technical improvement in Lange's colloidal gold test, *Jour. Michigan State Med. Soc.*, January, 1916.

The 1 c.c. pipettes should be graduated to the tip, otherwise two measuring points must be determined and time lost by returning the amount in excess of 1 e.c. to the preceding tube. It is well to see, too, that there is a wide margin between the 1 e.c. mark and the top of the pipette.

Although in the usual technic the concentration of the spinal fluid in the tenth tube is 1 to 5120, the ratio of the total volume to the volume of the colloidal gold employed is higher than in the other tubes, unless 1 c.c. is removed from the tenth tube and rejected. This point is not clearly brought out in the descriptions of the technic which have come under our notice, with the result that the curves obtained before making this correction had an upward "kick" at their ends which was rather misleading.

CONCLUSIONS. 1. That colloidal gold solutions which conform to every clinical requirement (differential paretic, luetic, tabetic, meningitic, and normal curves) may be made with comparative ease.

2. That it is quite unnecessary to use other than ordinary distilled water from any convenient laboratory still.

3. That nothing is to be gained by elaborate precautions in cleaning the glassware used, and that apparatus washed with soap and water, rinsed in tap water, and hung up to dry has been found entirely satisfactory.

4. That the reagents used may all be introduced at the beginning of the experiment, and temperatures other than the final one disregarded.

5. That providing sufficient oxalic acid is present the only critical points involved are the amount of formaldehyde used,<sup>12</sup> and the passing of the color transition point at which the solution lightens and becomes orange red.

6. That solutions so prepared were of the proper color and transparency and precipitated properly with a dilute electrolyte.

7. That if a thick layer of the solution is transparent, and of the proper color, a certain amount of surface dispersion is no bar to its usefulness.

## THE PRESENT STATUS OF HODGKIN'S DISEASE.<sup>1</sup>

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THE past five years have witnessed a wave of renewed interest in the subject of Hodgkin's disease. Inasmuch as the crest of this wave seems to have been reached, and possibly passed, it is perhaps

<sup>12</sup> This is in the vicinity of 17 per cent. of that recommended by Miller, Brush, Hammers and Felton.

<sup>1</sup> Read before the Chicago Society of Internal Medicine.

timely to review certain of the more important studies devoted to the condition with the view of determining, if possible, what of permanent value has been added to our knowledge.

**PATHOLOGICAL CLASSIFICATION.** Though Morgagni was the first to describe the clinical picture of this disease, the name of Hodgkin, who wrote *On Some Morbid Appearances of the Absorbent Glands and Spleen*,<sup>2</sup> is generally associated with the condition. As is commonly the case with first descriptions, Hodgkin's report included a variety of processes which today we know conclusively to belong elsewhere. For example, he grouped under a common heading not only cases of Hodgkin's disease in the strict sense, but also syphilitic and scrofulous tumors of the lymph nodes, metastatic carcinoma of the nodes, and still other conditions quite different pathologically from malignant granuloma.

Cohnheim, some thirty years later (1865), introduced the term pseudoleukemia as a fit one to portray the principal objective clinical feature of the same ill-defined group of diseases. In the light of our present considerably increased knowledge of the leukemias we can say, without fear of contradiction, that the name pseudoleukemia, whether applied to the motley group of diseases embraced by Hodgkin's report, or applied only to the well-demarcated condition called malignant, or infectious, granuloma, is a thoroughly unsatisfactory one, and should be reserved for the aleukemic leukemias of Türk,<sup>3</sup> with characteristic leukemic histological changes in the lymphatic tissues of the body, but unassociated with a leukemic blood picture.

The recognition of the true nature of Hodgkin's disease—using the term in the strict sense—as a granulomatous process with a fairly constant histological picture is a matter of scarcely more than fifteen years, and is associated with the studies of Sternberg,<sup>4</sup> Dorothy Reed,<sup>5</sup> McCallum,<sup>6</sup> Longcope<sup>7</sup> and others. We refer at this point not to the recognition of the particular form of the infection present, but in a general way to the fact that certain of the many conditions hitherto gathered under the inclusive caption of Hodgkin's disease were of the nature of granulomas and to be separated from the true leukemias, from sarcoma, from tuberculosis in its usual manifestations, and from syphilis.

As to terminology, we may conclude that we are justified in applying the term pseudoleukemia to the condition we are discussing only insofar as we imply that there exists a group of morbid

<sup>2</sup> Medico-Chirurg. Trans., 1832.

<sup>3</sup> Wien. klin. Wchnschr., 1903, xvi, 1073.

<sup>4</sup> Ztschr. f. Heilk., 1898, xix, 21; Centralbl. f. d. Grenzgeb. d. Med. u. Chir., 1899, ii, 641; also in Lubarsch-Ostertag, *Ergeb. d. allg. Path.*, etc., 1903 (1905), ix, Part 2, 360.

<sup>5</sup> Johns Hopkins Hosp. Reports, 1902, x, 133.

<sup>6</sup> Tr. Assn. Am. Phys., 1902, xxii, 350.

<sup>7</sup> Bull. Ayer Clin. Lab., 1903-4; *ibid.*, 1906, 86; *ibid.*, 1907, 18; also in Osler and McCrae's *System of Medicine*, 2d edition, 1915, vi, 755.

processes of quite different etiology and microscopic characteristics, having in common merely the chief objective clinical feature of lymphoid leukemia, namely, the more or less generalized enlargement of the lymph nodes. Hodgkin's disease is a distinctly preferable term, and is acceptable when employed in the restricted sense of malignant or, better, infectious granuloma. With our tendency to slight the historical in medicine it is as well to preserve, so far as possible, in our nomenclature the names of historical significance.

The clarification of the subject of Hodgkin's disease began, therefore, with the separation of the granulomatous members of the larger group from the lymphocytomatous, *i. e.*, the leukemias and the lymphosarcomatoses. The next period, and this includes the present, has concerned itself with investigations into the character of the underlying infectious process. We may consider this phase of the subject under two heads: (1) the relation of Hodgkin's disease to tuberculosis, and (2) the position of the so-called *Corynebacterium granulomatis maligni* in the etiology of the disease.

**HODGKIN'S DISEASE AND TUBERCULOSIS.** Since the publication of studies by Sternberg, in 1898, 1899 and 1905,<sup>8</sup> in which he describes a peculiar form of tuberculosis of the lymph nodes, many conflicting reports have appeared bearing upon the relationship of Hodgkin's disease to tuberculosis. The histological picture of the Sternberg cases differs in no important detail from that which we are accustomed to regard as characteristic of malignant granuloma, as portrayed by Dorothy Reed,<sup>9</sup> Longcope<sup>10</sup> and others. Yet, whereas Sternberg was able in 15 out of 18 cases to establish a tuberculous etiology either by direct staining of the affected nodes or by animal inoculation, Reed, Warnecke,<sup>11</sup> Yamasaki<sup>12</sup> and others were uniformly unsuccessful in proving such an association.

Sternberg believed the assumption of a tuberculous etiology to be strengthened by the fact that in certain of his cases tuberculosis existed elsewhere in the body, and that in still other cases typical tubercles were present in the same nodes showing the peculiar granulomatous tissue. To account for the latter on a tuberculous basis, Paltauf<sup>13</sup> assumed an infection with an attenuated bacillus, and Benda<sup>14</sup> one with the toxins of the tubercle. More recently, however, observers generally have inclined to the belief that the tuberculous process in the granulomatous nodes was either an associated or a superimposed infection and unrelated to the malignant granuloma.

A new trend was given to work along these lines when Fraenkel

<sup>8</sup> Loc. cit.

<sup>9</sup> Loc. cit.

<sup>10</sup> Loc. cit.

<sup>11</sup> Mitth. n. d. Grenzgeb. d. Med. u. Chir., 1905, xiv, 275.

<sup>12</sup> Ztschr. f. Heilk., 1901, xxv, 269.

<sup>13</sup> Ergeb. d. allg. Path. u. pathol. Anat., 1896, iii, 652; also in Mrazek's Handb. d. Hautkrankh., 1909, iv, Part 2, 681.

<sup>14</sup> Verhandl. d. Deutsch. pathol. Gesells., 1901, vii, 123.

and Much,<sup>15</sup> and in confirmation many others, isolated from lymph nodes showing the characteristic histological picture of infectious granuloma a granular, Gram-positive, antiformin but not acid-fast rod, which when injected into animals in the form of glandular emulsions produced in them typical tuberculous lesions. They called this organism, therefore, a granular form of the tubercle bacillus and believed it responsible for the peculiar histological picture of Sternberg.

In view of the recent bacterial studies devoted to Hodgkin's disease it would seem uncalled for, perhaps, to dwell at such length upon the role of the tubercle bacillus in the etiology of the condition. The matter cannot be entirely disregarded, however, (1) because the etiological association of any other known mycotic agent is still an open question, and (2) because careful workers are not wanting who continue to emphasize the relationship of the process to tuberculosis. Among others may be mentioned Steiger,<sup>16</sup> who, in 1914, published from the Eichhorst clinic a comprehensive clinical and experimental study in which he came to the not entirely novel conclusion that Hodgkin's disease was due to the bacillus of bovine tuberculosis. He apparently demonstrated, among other things, that patients with the disease who showed no response to any of the human tuberculin tests did react positively to the von Pirquet and Calmette tests when material from the bovine organism was used; and by employing glandular emulsions assumed to contain this organism, he reported that he was able to reproduce the typical granulation tissue in rabbits. It is possible that Steiger's results may be adduced in explanation of certain of the negative reactions in Hodgkin's disease obtained by observers who based their conclusions solely on the use of tuberculin from the human bacillus. This reasoning would not apply to negative inoculations tests in the guinea-pig, which, unlike the rabbit, is equally susceptible to the human and bovine organism.

To attempt to draw conclusions from these conflicting data bearing on the role of tuberculosis in the causation of Hodgkin's disease seems at present ill-advised, unless it be assumed, as suggested by some, that the typical granuloma of the disease is not of uniform etiology, but may be caused, on the one hand, by organisms still undiscovered, and, on the other, by the tubercle bacillus in one of the various forms already mentioned.

THE POSITION OF THE SO-CALLED CORYNEBACTERIUM GRANULOMATIS MALIGNI IN THE ETIOLOGY OF HODGKIN'S DISEASE. The history of the association of the pleomorphic, non-acid, but antiformin-fast organism, variously called a diphtheroid bacillus, the

<sup>15</sup> München. med. Wehnschr. (abstract), 1910, No. 10, 1035; *ibid.*, 1910, No. 13, 685; *Ztschr. f. Hyg.*, 1910, lxxvii, 159. Fraenkel: *Deutsch. med. Wehnschr.*, 1912, No. 14, 637.

<sup>16</sup> *Ztschr. f. klin. Med.*, 1914, lxxix, 452.

*Corynebacterium granulomatis maligni*, and by the less conservative *Baeterium hodgkini*, from the first description by Fraenkel and Mueh<sup>17</sup> to the later ones of de Negri and Mieremet,<sup>18</sup> Bunting and Yates,<sup>19</sup> Billings and Rosenow<sup>20</sup> and others, is too recent to require recapitulation. The opinion of Fraenkel and Mueh as to the tuberculous character of this organism has already been alluded to. In this particular they differ from the great majority of later observers. Of the latter, Bunting and Yates have gone furthest in emphasizing the specific etiological character of this diphtheroid bacillus in Hodgkin's disease. For a time, indeed, their enthusiasm seemed well-founded, what with the occurrence of the organism, in one form or another, in practically all of their cases, their ability to obtain it in pure culture and their apparent success in transferring the disease in characteristic form to the rhesus monkey.

Since attention was first directed to this diphtheroid bacillus its presence in the granulomatous tissue has been amply verified. Positive reports far outnumber negative. Bunting and Yates, we believe, have demonstrated it in every one of their cases; while Billings<sup>21</sup> has recently reported that it was found in 40 out of 42 of his series.

This striking regularity of occurrence was at first naturally looked upon as very strong evidence of the specific etiological role of the diphtheroid bacillus. Recently, however, studies have accumulated which seem to take from this point much of its apparent weight. The following considerations merit special emphasis:

1. A diphtheroid organism has been found in a number of conditions seemingly unrelated to Hodgkin's disease. Steele,<sup>22</sup> and also Simon and Judd,<sup>23</sup> isolated the bacillus from the lymph nodes of lymphoid leukemia; Rosenow<sup>24</sup> has found it in arthritis deformans and in goiter, and Bunting<sup>25</sup> in chronic leukemia, lymphosarcoma, chloroma, Banti's disease, etc. In a case of von Recklinghausen's disease reported by Charles Elliott and the writer<sup>26</sup> the diphtheroid organism was apparently present in some of the subcutaneous nodules. It would appear that Bunting and Yates<sup>27</sup> have receded materially from their original emphatic stand relative to the specific nature of this bacillus in conceding that it is found in a number of conditions other than Hodgkin's disease. They assuredly do not

<sup>17</sup> Loc. cit.

<sup>18</sup> *Centralbl. f. Bakt., orig.*, 1913, lxxviii, 292.

<sup>19</sup> *Arch. Int. Med.*, 1913, xii, 236; *Jour. Am. Med. Assn.*, 1913, lxi, 1803; *ibid.*, 1914, lxii, 516; *Bull. Johns Hopkins Hosp.*, 1914, xxv, 177.

<sup>20</sup> *Jour. Am. Med. Assn.*, 1913, lxi, 2122.

<sup>21</sup> Quoted from an abstract of the *Tr. Assn. Am. Phys.* (1916), in *Jour. Am. Med. Assn.*, 1916, lxvi, 2031.

<sup>22</sup> *Boston Med. and Surg. Jour.*, 1914, clxx, 123.

<sup>23</sup> *Jour. Am. Med. Assn.*, 1915, lxiv, 20, 1630.

<sup>24</sup> *Ibid.*, 1914, lxiii, 903.

<sup>25</sup> *Bull. Johns Hopkins Hosp.*, 1915, xxvi, 179, 376.

<sup>26</sup> *Jour. Am. Med. Assn.*, 1914, lxiii, 1358.

<sup>27</sup> *Bull. Johns Hopkins Hosp.*, 1915, xxvi, 179, 376. Also *Tr. Assn. Am. Phys.* (1916), abstracted in *Jour. Am. Med. Assn.*, 1916, lxvi, 2031.

strengthen their position by maintaining that those diseases in which the bacillus has been found—leukemia, lymphosarcoma, etc.—are genetically related because the same organism may be common to all. Finally, as pointed out by Bloomfield,<sup>28</sup> a diphtheroid bacillus may be present in lymph nodes which are apparently in normal condition.

2. In addition to the diphtheroid bacillus, other organisms are not infrequently found in Hodgkin's gland. Thus Rosenow,<sup>29</sup> while able to cultivate the diphtheroid bacillus from all of 40 cases, found in 17 of these cases a staphylococcus, in 7 the *Streptococcus viridans*, in 14 an organism resembling *Bacillus welchii*, and in 6 Gram-negative bacilli. The coexistence of the diphtheroid bacillus and the tubercle bacillus has already been commented upon.

3. Immunological studies have cast serious doubt upon the specific character of the organism in question. Olitsky,<sup>30</sup> and more recently Moore,<sup>31</sup> were able to obtain what appeared to be satisfactory antigens in their work, and yet in only one of their cases, this being one of Moore's series with syphilis in addition, did they observe fixation of complement. Nor, in the process of active immunization with these organisms, did Moore obtain an increase in the specific agglutinative power of his patients' sera. These findings, while not conclusive, are highly suggestive, for with a satisfactory antigen one may look for the fixation of complement if the antigen be specific.

4. The cultural studies of Bloomfield:<sup>32</sup> Bloomfield, in a mixed series of cases, some with practically normal lymph nodes, others with a distinct pathology, isolated 29 different strains of organisms. More positive cultures were obtained from diseased than from relatively normal glands. No correlation was evident between a given organism and a specific tissue change. The relative avascularity of the lymph-glandular tissue possibly predisposes to the localization of microorganisms, some of which may be traced to contiguous infections while others are saprophytic and correspond to the flora of the body surfaces. Belonging to the latter class is the pseudodiphtheria bacillus, which would account for its occasional presence in normal glands and its frequent or, as the case may be, regular occurrence in pathological tissues which favor its growth.

As to the conveyance of the disease to animals, reports are not entirely in accord. Bunting and Yates have stated that it was possible to reproduce the disease in typical form in the monkey, regularly, provided the organism injected was not too virulent and the injections not too frequent to cause the early death of the animal. Moore,<sup>33</sup> on the contrary, was unable to produce a lesion

<sup>28</sup> Arch. Int. Med., 1915, xvi, 197.

<sup>29</sup> Jour. Am. Med. Assn., 1914, lxi, 903.

<sup>31</sup> Jour. Infect. Dis., 1916, xviii, 569.

<sup>32</sup> Loc. cit.

<sup>30</sup> Ibid., 1915, lxiv, 1134.

<sup>33</sup> Loc. cit.

resembling that of Hodgkin's disease in his work. Rhea and Falconer<sup>34</sup> had obtained no results in the conveyance of the disease to a monkey up to the time their paper was published, and no further report, so far as we know, has come from them. Lanford,<sup>35</sup> using the guinea-pig, was likewise unsuccessful. And, finally, the entire matter is further obscured by the work of Steiger,<sup>36</sup> already referred to, in which by means of the bacillus of bovine tuberculosis, he produced the granuloma in the rabbit.

Though the question of the relation of the diphtheroid organism cannot be called a settled matter, the evidence against its being the specific cause of Hodgkin's disease is constantly increasing, so that we are perhaps not premature in concluding that little of the original contention of Bunting and Yates has stood the test of recent studies.

Of less importance than the foregoing matters, but perhaps worthy of mention at this time because of the emphasis laid upon it by some, is the subject of the blood picture in Hodgkin's disease. The extreme position here, as in the case of the diphtheroid organism, has been taken by Bunting and Yates. The former<sup>37</sup> has maintained that he was able to make a highly probable diagnosis of the condition merely by the examination of the blood smear, the most characteristic feature, according to him, being, as is well known, a relative, and, as a rule, also absolute increase in the large mononuclear and transitional cells. Bunting's data indicate that such an increase is present throughout the course of the disease, as a rule, but we believe that special emphasis has been laid upon the mononuclear increase in the early stages. The other suggestive findings, according to Bunting, are the increase in the number of blood platelets, many of which are abnormally large, and the presence of detached pseudopodia of megalokaryocytes. Bunting is in accord with observers in general with respect to the other characteristics of the leukocytic blood picture, namely, a practically normal white cell count—or, possibly a slight leukopenia or a slight leukocytosis—in the early stages of the disease, and a variably high leukocytosis of the polynuclear type with a marked and progressive diminution of the lymphocytes in the advanced stages. An eosinophilia, in addition, may be present.

In the literature subsequent to the appearance of Bunting's articles on this subject we have been able to find only the most meager reference to the matter of blood platelets and megalokaryocytic pseudopodia. As to the increase in the large mononuclear and transitional cells there seems to exist a considerable difference of opinion. Steiger reports a relative lymphocytosis in the

<sup>34</sup> Arch. Int. Med., 1915, xv, 438.

<sup>35</sup> New Orleans Med. and Surg. Jour., 1915, lxxvii, 983.

<sup>36</sup> Loc. cit.

<sup>37</sup> Bull. Johns Hopkins Hosp., 1911, xxii, 114, 369; *ibid.*, 1914, xxv, 173.



early phases of the disease, a marked polynuclear leukocytosis in the most active middle period, and a progressive diminution of the lymphocytes as fibrosis advances. Billings and Rosenow speak of a moderate leukopenia with a relative increase of the small mononuclear cells in some of the afebrile patients and of a leukocytosis with the usual leukocytic formula in most of the febrile patients. Moore<sup>38</sup> found in an inoculated monkey an average large mononuclear count of 4.79 per cent. as against a percentage of 10.73 per cent. as recorded by Bunting and Yates in their animal work. Naegeli<sup>39</sup> and others, on the contrary, regard an increase in these cells as of frequent occurrence in Hodgkin's disease.

Thus in this matter, as in the majority of the other subjects we have considered, there is no unanimity of opinion. However, we believe that hematological studies warrant the following conclusions regarding these cells:

An increase, when present, does not point to a specific reaction of the Hodgkin process upon the structures of the lymph nodes, because the great preponderance of evidence goes to show that the large mononuclears arise not in the germinal centers of the lymph glands, as is maintained by some, but are products of the myeloid system.<sup>40</sup> Neither in Hodgkin's disease nor in any other condition do these cells run parallel to the lymphocytes. On the contrary, it has been amply shown that they increase and decline in number, *pari passu*, with the other cells of the granular system. In the second place, Hodgkin's disease is not the only condition producing destructive changes in lymph nodes which is associated with an increase in the cells in question. A similar increase is seen not infrequently in tuberculosis and in metastatic carcinoma of the lymph nodes, for example. It would appear, therefore, that the percentage increase in the large mononuclears and transitionals is rather a bone-marrow than a lymph-node reaction, and has the same significance in Hodgkin's disease as does the increase in the polynuclear neutrophils, the eosinophilia, and the presence of occasional myelocytes, namely, the bone marrow response to infections in general.

A final word as to treatment. In a process of this kind, which is in all likelihood of an infectious nature, progress in treatment may be expected to go hand in hand with an increased knowledge of the character of the infectious agent. Our early hopes in vaccine therapy have declined with our increasing doubt of the specificity of the so-called *Corynebacterium hodgkini*; and, although we still hear of cures which derive apparent benefit from vaccines, we believe that this method of treatment is gradually falling into disuse. Surgical intervention offers hope in no greater degree, perhaps,

<sup>38</sup> Loc. cit.

<sup>39</sup> Blutkrankh. und Blutdiagnostik, 2d edition (1912), 187.

<sup>40</sup> In this connection see the recent work of Evans: Arch. Int. Med., 1916, xvii, 1.

than in malignancy, namely, insofar as the affected tissues can be removed completely, which is rarely possible. If the Hodgkin process can be conclusively linked with a definite source of infection, and that source be eradicated before the disease has made too great progress, a cure may perhaps be hoped for. Meanwhile we must content ourselves with our earlier methods, namely, arsenic, the roentgen rays, and possibly radium.

## ASTHMA CONSIDERED IN ITS RELATIONSHIP TO THE VEGETATIVE NERVOUS SYSTEM.<sup>1</sup>

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WITH our more extended knowledge of visceral neurology we are able to form more definite ideas regarding so-called visceral neuroses; and such conditions as hay fever, asthma, hyperchlorhydria, and spastic constipation can now be studied from a standpoint which offers to help solve many of the questions regarding them which have heretofore been misunderstood. These various clinical manifestations have been heretofore classed among the diseases of the organ or part affected, but our newer knowledge makes it plain that this is a mistake. They are evidences of reflex action. These phenomena are manifestations in different organs of the same syndrome, that of increased vagus stimulation. To make this clear it is only necessary to recall our physiology.<sup>2</sup>

THE VEGETATIVE OR INVOLUNTARY NERVOUS SYSTEM. That part of the nervous system which is not under direct control of the will is called the vegetative or involuntary, sometimes also the autonomic. It supplies:

1. The subdermal musculature (pilomotor muscles and muscles of sweat glands).
2. Heart and bloodvessels.
3. Muscles and glands of the respiratory tract.
4. Muscles and glands of the gastro-intestinal tract, including the salivary glands, liver, and pancreas.
5. Genital tract.
6. Urinary tract.
7. The ciliary body, pupil and lacrimal gland.
8. All other smooth muscle and glandular structures of the body.

<sup>1</sup> Read before the Thirty-fourth Annual Meeting of the American Climatological and Clinical Association, Lakewood, N. J.

<sup>2</sup> Pottenger: The Vegetative Nervous System in Relation to General Medicine. Read at Annual Meeting of California State Medical Society at Coronado, April 17-19, 1917, California State Jour. of Med., November, 1917.

Throughout the entire body the principle of action and counter-action is evident. This we see in the flexors and extensors, in inspiration and expiration, and in vasoconstriction and vasodilatation. Normal function is preserved by maintaining an equilibrium between the acting and inhibiting forces.

The vegetative nervous system is divided into two distinct divisions: one originating in the medulla, bulb, and sacral portion of the cord, the other in the thoracic and upper lumbar segments of the cord. These two divisions are antagonistic to each other. They each give fibers to most of the important internal viscera and structures, including the heart, possibly some bloodvessels (all receive sympathetic fibers), bronchi, stomach, intestines, liver, pancreas, and genital and urinary organs. In each structure supplied by both, one produces action, the other inhibition. That division coming from the thoracic and upper lumbar segments of the cord is called the sympathetic nervous system; the other is called the *greater vagus*. The term greater vagus is applied to all the vegetative fibers that do not belong to the sympathetic system, and is named for the tenth cranial nerve, which is the most extensive nerve in its distribution of the division. It comprises the vegetative fibers in the third, seventh, ninth, and tenth cranial and those in the pelvic nerve. When these two divisions of the vegetative nervous system are in normal tone, normal physiological action takes place; but when one is overstimulated the equilibrium is destroyed and pathological action results.

**ANTAGONISTIC ACTION OF THE SYMPATHETIC AND GREATER VAGUS DIVISIONS OF THE VEGETATIVE SYSTEM.** The antagonism of these two systems shows in the following manner in a few of the more important structures of the body.

*Eye.* Sympathetic dilates pupil and contracts Müllerian muscle, greater vagus contracts ciliary body and pupil and increases lacrimation.

*Salivary Glands.* Sympathetic decreases secretion; greater vagus increases secretion.

*Stomach.* Sympathetic decreases motility and secretion, including hydrochloric acid; greater vagus increases motility and secretion, including hydrochloric acid.

*Intestines.* Sympathetic decreases secretion and motility; greater vagus increases secretion and motility.

*Liver and Pancreas.* Sympathetic decreases secretion; greater vagus increases secretion.

*Nose and Accessory Sinuses.* Sympathetic constricts vessels, decreases sensibility and decreases secretion; greater vagus dilates vessels, increases sensibility and increases secretion.

*Bronchi.* Sympathetic relaxes muscle tone and decreases secretion; greater vagus causes spasm of bronchial musculature and increases secretion.

*Heart.* Sympathetic increases rapidity of action; greater vagus slows.

*Bloodvessels.* Sympathetic causes vasoconstriction; greater vagus in some parts causes vasodilatation.

*Blood-forming Organs.* While it is not possible to be definite in this matter, yet it has been noticed that conditions which cause increased sympathetic stimulation are accompanied by leukocytosis, with the increase largely in the number of neutrophiles; while those conditions which cause increased stimulation of the greater vagus are accompanied by increased lymphocytosis, eosinophilia and decreased coagulability of the blood.

ASTHMA A PART OF THE SYNDROME OF INCREASED GREATER VAGUS STIMULATION. With these physiological considerations it is evident that the symptoms of asthma belong to a group which results when the greater vagus is overstimulated. The principal symptoms of asthma are dyspnea and cough. These are due to an increased secretion in the glands of the bronchial mucous membrane and a spasm of the bronchial musculature. Emphysema is also an accompaniment in many cases. There is also commonly an increase in eosinophiles in the sputum. This picture is clearly that of overstimulation of the vagus.

The rapid heart is due to sympathetic stimulation and shows how Nature in her effort to preserve the individual provides that the essential body functions be carried on. In asthma we would expect the heart to be slower than normal if the same vagus stimulation extended to the cardiac vagus, but if it did, life would be endangered by failure of oxygenation; so, as diminished oxygenation results in acid retention, the vasomotor center in the brain is stimulated and vasoconstriction with increased rapidity of heart beat takes place and a partial equilibrium is maintained. While oxygenation may not be fully carried on, in fact rarely is, yet a degree which is sufficient to meet the immediate necessities is usually established and maintained until the emergency is passed.

Medical literature is filled with speculation regarding the cause of asthma. Many have thought that the associated bronchitis must be the cause. This idea has been strengthened by the fact that the secretion lessens as the spasm lessens. This may be explained, however, by the fact that both spasm and increased secretion are results of vagus stimulation. We are not in a position to say, however, that the presence of the secretion on the mucous surface does not further irritate the vagus endings and prolong the attack. This is possible. It is also possible that vagus stimulation might call forth a different response in the muscle fibers and the secretory glands according to the strength or other characteristics of the stimulation. The one fact that is of prime importance in understanding the nature of asthma is that the essential conditions, bronchial spasm, increased bronchial secretion and cough (dyspnea and emphysema being

results), likewise the increase of eosinophiles in the sputum, are conditions which are met when the equilibrium in the vegetative nervous system is disturbed in such a manner that vagus tonus predominates.

There are also, doubtless, changes in the glands of internal secretions which result from this disturbed equilibrium. What they are and whether they are within normal limits of variation we do not know, but must leave for further study.

That vagus stimulation is the factor which is accountable for the symptoms cannot be doubted. This is the reason why atropin and adrenalin are the remedies of greatest value for relieving the asthmatic attack. Atropin depresses the action of the vagus, and if it could be given in doses sufficiently large would undoubtedly relieve asthma; but its drying effect on the secretions is so marked that doses which are required for the relaxation of the bronchial spasm cause too great discomfort.

Adrenalin opposes the action of the vagus by producing the same effect in the tissues as would result from central stimulation of the sympathetics. I have listened through the stethoscope to a severe attack of asthma accompanied by many squeaks and rales, and note it disappear and the breathing become smooth and almost free from asthmatic signs within three minutes after the injection of 20 minims of a 1 to 1000 solution of adrenalin.

Another observation which tends to show definitely that asthma is due to vagus stimulation is the manner in which asthma is at times influenced by toxemia. Toxins cause an increased tonus in the sympathetic system.<sup>3</sup> Several patients who have come under my care have been relieved of asthmatic attacks by intercurrent infections—one by a tonsillitis, another by tuberculous toxemia, and a third by a pneumonia. These I have discussed more fully elsewhere.<sup>4</sup> Whether a case will be relieved by atropin, adrenalin, or by such intercurrent toxemias as just mentioned depends upon whether or not the sum total of the sympathetic stimulation or the depressing action as produced by atropin is able to counteract and inhibit the increased vagus tonus.

**CAUSES OF INCREASED TONUS IN THE PULMONARY VAGUS.** *Vagotonic Disposition.* The first fact bearing on this point is the one which has been emphasized in vague terms for many years, without any definite conception of its meaning, namely, that there is a certain inherited nervous basis back of asthma. Studies in visceral neurology show what this is. Eppinger and Hess<sup>5</sup> have particularly visualized this condition under the term "vagotonia." While equilibrium is maintained in the structures supplied by the vegetative system by the tonus in the sympathetic nerves equal-

<sup>3</sup> Pottenger: The Syndrome of Toxemia, Jour. Am. Med. Assn., January 8, 1916.

<sup>4</sup> Pottenger: Clinical Tuberculosis, C. V. Mosby Co., St. Louis, 1917.

<sup>5</sup> Vagotonia, English Trans. Nervous and Mental Disease Pub. Co., 1915.

ling the tonus in the greater vagus there are many individuals in whom the balance is slightly or markedly on the vagus side. If not already on that side it may be thrown to it by any extra irritation of the nerve centers by which their threshold of response is lowered. This often follows overwork, disease, worry, discontent, and other depressive emotions and the neurasthenic and psychasthenic states. While nerve equilibrium may be maintained under ordinary, favorable states it is quickly destroyed by conditions which produce harmful stimulation of the nerve centers. A vagotonic may not show the complete syndrome of vagotonia. Only one or a few structures may show the influence of overstimulation. Thus one patient may have increased irritability of the lacrimal glands and nasal mucous membrane and show hay fever; another of the bronchi and suffer from asthma; while still others may show the symptoms most marked in the gastro-intestinal tract and suffer from hyperchlorhydria, spastic constipation, and intestinal stasis.

We conceive that a patient who is distinctly vagotonic might have not only a widespread predominance of vagus stimulation but also increased tonus, the expression of which is limited to one or more branches of the greater vagus. When limited to the pulmonary branches asthma results. It is not beyond conception that asthma might exist because of a specially low threshold of response in the cells which give origin to the pulmonary branches of the greater vagus in an individual who is decidedly vagotonic. Under these conditions a much less stimulus is adequate than under conditions of normal nerve tonus. In spite of this assumption, however, I am convinced that when the etiology is carefully worked out that we shall find that either peripheral irritation of the pulmonary vagus endings or reflex stimulation from irritants affecting filaments of the greater vagus in other internal viscera will be found to be the predominant factors which increase the already existing predominant vagus tonus.

It has long been supposed that the gastro-intestinal canal is specially liable to be the source of reflexes which cause asthma. Bearing on this point I should call attention to the fact that embryologically the lungs are formed from a diverticulum from the intestine. This fact makes the respiratory and digestive tracts closely associated in their innervation. In my study of pulmonary tuberculosis I have found this fact very evident. The inflammation in the lung apparently causes reflex stimulation in the gastric and intestinal branches of the vagus more regularly than in any other structures outside of the respiratory tract.

Let us now turn our attention more particularly to the study of those factors which might either directly or reflexly cause increased pulmonary vagus stimulation and precipitate the syndrome recognized in asthma.

*Causes Acting Directly on the Pulmonary Vagus.* It seems to me that it is probable that the condition of the atmospheric air is a factor in the production of asthma. Observation of a number of asthmatics at the same time (in Southern California) has shown me that while all will not suffer attacks at the same time, yet several will; and further, that the attacks seem to be precipitated by changes in weather. The factors in the atmosphere which seem to be potent in producing the attacks are apparently more active during changes from normal humidity to increased dryness or increased dampness. It would seem that the musculature and mucous membrane of the bronchi are not able to adjust themselves readily to the changes and that irritation results. Fog at times is sufficient to produce the adequate stimulus for an attack. Those who have leaned toward the theory that asthma is due to bronchitis have explained the attacks following foggy and damp weather as being due to an increased bronchitis.

It may be that dust and other irritants in the atmosphere are also factors in some cases. The action of all of these factors may be either direct on the pulmonary vagus, or, what seems more reasonable, upon the nerve endings in the upper air passage and larger bronchi, the asthma being a result of the reflex.

Asthma, now and then, seems to be due to direct irritation of the pulmonary vagus from conditions within the thorax. I have seen attacks follow rapidly forming fibrosis in tuberculosis, either with or without marked shifting of the diaphragm. It seemed that the direct irritation of the vagus endings in the lung was most probably the determining factor, yet we cannot exclude the possibility of protein irritation resulting from the change in the pulmonary tissue.

*Causes of Reflex Stimulation of the Pulmonary Vagus from Other Viscera.* Irritations which occur in the upper air passages have just been mentioned, but there are many sources of reflexes which may cause increased tonus in the pulmonary vagus.

Asthma sometimes accompanies hay fever. In this case it would seem that what irritates the nerve endings of the upper air passages locally stimulates the pulmonary vagus reflexly.

Deflected septum, pressure, polypi, and sinus infections at times cause asthma. The chief factor in each of these conditions seems to be a reflex stimulation, although in case of polypi and sinus infections so-called protein poisoning may be a factor, as will be evident as our discussion proceeds. Irritation in the nose, however, may be a result of the same vagus stimulation as that which produces the asthma instead of being an exciting cause of the asthma.

Next to the respiratory tract, for embryological reasons, as previously mentioned, irritation in the gastro-intestinal tract should be the most apt to cause reflex stimulation in the pulmonary vagus, and this has long been believed. Cardiac asthma is also spoken of; and we now and then see cases reported in which the

reflex cause seemed to be in the genital or urinary tracts. The various neurons of the greater vagus are closely bound through the ascending and descending fibers in the cord, so that stimulation may excite reflexes in far distant organs. We know vomiting may be reflexly caused by ovarian and uterine irritation; why not asthma as well?

*Anaphylaxis.* There has been a growing tendency in recent times to appreciate more fully than formerly that the body tissues often find themselves confronted with foreign substances which have passed through the normal protective defences. Thus foreign substances may pass through the mucous membranes of the upper air passages, and undigested food may pass the protective cells of the intestinal mucous membranes. In the destruction of these foreign substances certain reactions occur. One is recognized as toxic, another as anaphylactic; the former expresses itself through the sympathetic portion of the vegetative nervous system, the latter through the greater vagus. These I have discussed more fully elsewhere.<sup>6</sup>

When the substance which enters the tissues of the body is a foreign protein, sensitization of the body cells takes place. When the same protein enters again the cells are better able to destroy it because they are endowed with the power of producing specific defence. The destruction of the protein is accomplished by biochemical reaction. As a result nerve endings are irritated. When nerve endings of the vegetative nervous system in internal viscera are irritated the sympathetics cause segmental reflexes through the sensory and motor spinal nerves, while the greater vagus filaments cause reflexes in other internal viscera. Protein in the process of being broken up circulates in the tissues and may irritate the nerve endings of one branch of the greater vagus more than another.

The biochemical reactions which are associated with the parenteral elaboration of foreign protein cause the syndromes of toxemia and anaphylaxis. These are closely related to reactions which result from the breaking down and elaboration of native protein during inflammatory processes. Here we have foreign protein also in all cases of infectious inflammation. In the destruction and elaboration of the protein of one's own tissues during inflammation the syndrome of toxemia is often present. The reaction which seems to be more particularly due to the cleavage and further elaboration of the non-toxic protein molecules expresses itself not as the syndrome of acute anaphylaxis, but, in more or less widespread vagus reflexes, in other organs. The syndrome which is recognized as anaphylaxis, either acute or chronic, and the symptoms indicative of vagus stimulation which result from visceral inflammation, seem to be

<sup>6</sup> Pottenger: The Relationship of the Syndrome of Anaphylaxis to the Vegetative Nervous System. Read before American Association of Immunologists, April, 1917, New York Med. Jour., August 18, 1917.



related, but the latter, as a rule, are less acute than the former. It is possible that the only difference may be the greater part taken by the cells in defending the body against foreign protein.

It has been my observation that patients who show increased tonus in the pulmonary branches of the greater vagus (asthma) are prone to have increased vagus tonus in one or more other organs. Hay fever, hyperchlorhydria, spastic constipation, and intestinal stasis are commonly found in patients who suffer from asthma.

Study of asthma in relationship to the vegetative nervous system shows it to be, in all probability, a condition with a varied etiology. In closing I wish to quote my conception of asthma from one of my recent discussions:<sup>4</sup> "Asthma is a disturbance in function. It is an increase in tonus of that portion of the greater vagus nerve which supplies the bronchial musculature and mucous membrane. Its cause may be as diverse as the irritants which may be applied to the nerve centers which give origin to the pulmonary fibers or to the peripheral nerves that are in reflex relationship with them. As all toxemias which are sufficiently severe may produce the toxic syndrome, so all irritations, either reflex or central, which produce sufficient stimulation of the nerve cells giving origin to the pulmonary filaments of the vagus may produce asthma."

<sup>4</sup> Pottenger: Loc. cit.

# WAR MEDICINE

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## WAR NEUROSES AND PSYCHOSES.<sup>1</sup>

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UNDER contemporary conditions of warfare the subject of nervous and mental disorders assumes much greater importance than ever before in military psychiatry.

In addition to familiar pathological states found in civilians and soldiers alike, in peace and war, there have developed various peculiar conditions for which new names have been found. Together they

<sup>1</sup> This article was contributed for the Manual of War Medicine which was to be edited by the late Dr. Lewis A. Stimson, but owing to the death of Dr. Stimson the publication had to be abandoned.

constitute the *war neuroses*. These conditions, while presenting nothing absolutely new in symptomatology, have nevertheless an individuality of their own precisely in the sense that their exciting causes and the circumstances under which they develop have never hitherto existed.

*Frequency.* The Surgeon-General's report covering the year 1915 shows that 25.6 per cent. of all discharges from the service were due to nervous and mental disease. In war, although the actual number of these diseases multiplies, the percentage decreases in the presence of the mounting casualties. Among Canadian soldiers invalided home, 1915-1917, they have constituted approximately 10 per cent.<sup>2</sup>

Another war difference is in the general type of disorder. During peace psychoses far outnumber the neuroses (8 to 1, U. S. Army, 1915). In war the relations are reversed, neurotic reactions making up 50 to 60 per cent. of the total nervous and mental disabilities.

The chief interest of war psychiatry is therefore in the neuroses. Their discussion should be prefaced, however, (1) by a statement of certain general characteristics of war psychopathology, and (2) by brief mention of the commoner psychoses and defect states which medical officers may be called upon to handle.

*Fallacious Sense Perceptions.* The circumstances leading to illusions and hallucinations of sight and hearing, and their types, are too obvious to require mention. The strained listening and watching by day, and particularly by night, especially when combined with physical exhaustion, are only too prone to render the evidence of the senses misleading.

Closely related are *battle dreams*, in which the patient again and again lives through his most harrowing experiences. *Somnambulistic and waking dream states* are not infrequent. In these all the maneuvers of conflict may be enacted, and unless safeguarded the invalid may injure others or come to grief himself by rushing into exposed places or charging headlong into some natural obstacle, *e. g.*, the wall of the room.

*Special Delusional Trends.* In depressive states, in which a civilian might harbor ideas of sin, moral delinquency, etc., the soldier reproaches himself with cowardice, failing in his duty, or takes undue blame for some disaster.

Men by nature suspicious, oversensitive, or in any way peculiar, are badly off in the army. Camp and field life is not tempered to them, and they may easily become victims of thoughtless teasing. From the individual's point of view this may amount to actual persecution, which, according to circumstances, he may pathologically exaggerate and grotesquely elaborate.

The spy delusion is quite common. The most damning thing that can be said of a man is that he is an enemy spy. Consequently the suspicious soldier easily becomes obsessed with the idea of being so regarded, especially if he has been subjected to actual teasing on account of enemy ancestry or a suggestive name. Incipient paranoiacs often express this delusion.

<sup>2</sup> This figure includes bullet and shell wounds of the skull, with or without brain lesions, representing about 1.5 per cent. of the total discharge disabilities.

*Malingering.* The practice of deception in one form or another, including self-deception, is very common. The habit of parading sick to avoid distasteful duty begins in camp and continues at the front for the same reason. It is perhaps hardly likely that the experienced medical officer will err on the side of overcredulity toward questionable disabilities. But unfortunately the skeptical attitude is sometimes overworked. Men have been undeservedly court-martialed and shot, as examples, through too-ready assumption of malingering.

It may be useful to distinguish the following conditions.

1. *Simulated Malingering.* This refers to certain pathological mental states with partial or complete irresponsibility, *e. g.*, early dementia precox, in which the symptoms themselves may suggest feigning.

2. *Exaggeration and Perseveration.* In actual disabilities symptoms are readily exaggerated subjectively, usually inversely to the gravity of the cause. This may be partly a voluntary matter, partly a temperamental reaction, and is not confined to the army. Still there is a lesson in the story of an old R. A. M. C. officer who is said to have handled his sick parade by giving treatment to all the odd numbers and returning the even numbers to duty.

Perseveration means the indefinite continuation of symptoms after the original cause has subsided. Habit tendencies here play a part. In conditions accompanied by pain perseveration may extend over many months, with no discoverable basis. Pain being a sensation which in many cases comes and goes at suggestion, the eventual question is, to what degree is the invalid himself persuaded of its existence? Again, in joint conditions, with original limitation or suspension of movement from whatever cause, voluntary motion may remain in abeyance indefinitely, without any anatomical or neurological grounds. Wherever advantage may accrue it would appear that perseveration may take place with a minimum of conscious participation.

3. *Hysterical Autosuggestion.* In this it is unnecessary to assume any organic lesion whatever underlying the symptoms presented. Many of the so-called shock symptoms, aphonia, deafness, paralysis, contractures, stammering, etc., belong in this category. The psychogenesis of these manifestations is that of hysterical symptoms in general.

4. *Mental Contagion.* Suggestion plays a self-evidently large part in war psychopathology. In its simplest form it amounts to nothing more than purposive collusion or limitation. It has happened, for example, that numbers of men in the same battalion have developed the same form of dermatitis, at about the same time, and from the same irritant self-applied.

Less directly conscious imitation is notoriously effective in the production of neurotic symptoms. Charcot's hysterics all followed more or less the same pattern. The specialist who is interested in any particular neurotic manifestation is likely to find it in all his patients. There is a conspicuous similarity in the symptomatology of the war neuroses which may be attributable partly to like causes.

5. *Voluntary Fabrication.* A not uncommon attempt to short-cut from active duty or awarded punishment is by way of feigned or artificial disability. A bare catalogue of these simulated conditions would make a long chapter.

They include factitious skin eruptions, abscesses and ulcers; con-

tusions, erythematous infiltration from self-inflicted blows repeated at intervals; picric acid jaundice (the French call these malingerers "carrots"); self-inflicted bullet wounds (also occasionally in dementia precox); edema of extremities from constricting bands (even to the degree of resembling elephantiasis); hemoptysis from pricking the throat; conjunctivitis from application of ipecac, tobacco, etc., repeated until chronic hyperplasia and scarring, even ectropion results; simulated otitis media by introduction of pus-like substances or genuine inflammation from instillation of irritants (sometimes a *bona fide* otitis furnishes the cue for an artificial disabling exacerbation); gastritis and gastro-enteritis from the ingestion of noxious substances; disordered action of the heart from swallowing tobacco; artificial diabetes; simulated pain and stiffness of joints; feigned amnesia, deafness, blindness, convulsions, automatism.

In dealing with any case of supposed malingering it is paramount to give careful attention to the mental state of the suspect. After eliminating actual mental disease a degree of psychopathic inferiority or defect with diminished responsibility may be demonstrable.

We pass to a review of the principal mental diseases encountered in the service.<sup>3</sup>

**DEMENTIA PRECOX.** Slowly developing psychosis: Apathy, inertia, defective sense of personal identity, feelings of control by external agents (electricity, hypnotism, etc.), aural hallucinations (abusive voices), irrelevant and incoherent thought and action, with inappropriate emotional expression, meaningless smiling, frequent response "I don't know" to questions, purposeless impulsive (often dangerous) acts, suspicious attitude toward comrades, with morbid self-centering.

Several points deserve special mention:

1. In the first place, dementia precox is by far the commonest psychosis occurring in the service in peace or war (at least 60 per cent. of all insane cases according to King). This preponderance is due to the fact that the usual age of onset coincides with the military age; and, further, to the nature of the precox constitution itself, a certain number of potential schizophrenics constantly drifting into the service.

2. In cases of suspected malingering, insubordination, repeated petty crimes and irresponsibility and inefficiency in general it should first be determined whether or not the delinquency is symptomatic of this disease. The behavior of precox patients in the early stages, their trifling evasive responses or sullen indifference, together with a tendency to alcoholic excesses, neglect of duty and frequent vague physical complaints, may easily arouse the suspicion of wilful perverseness or simulation.

3. Recognition of the psychosis may be delayed by a practically complete remission of symptoms, which may thus lend weight to the suspicion of malingering. Even when symptoms have become conspicuous and a medical board has certified the presence of mental disease, a second board, sitting a few weeks later, may be unable to find any abnormality and pronounce the man sane and fit. In due time a second revision of opinion of course becomes necessary.

<sup>3</sup> For an excellent presentation of military psychiatry in time of peace consult King's Mental Disease and Defect in United States Troops, War Department Bulletin No. 5, Government Printing Office, Washington.

**MANIC-DEPRESSIVE PSYCHOSIS.** Psychosis characterized by recoverable phases of emotional depression with feeling of incompetence and varying degree of inhibition in thought, speech and action on the one hand, and exhilaration, hyperactivity and talkativeness on the other. These phases may occur independently or in succession. Sometimes the symptoms of both are mingled.

Although transitory episodes of motor excitement under shell fire are sometimes observed, true mania or depressive syndromes are comparatively rare in the army, the latter being the more frequent.

Depressed cases may become self-accusatory and seek punishment for alleged crimes or dereliction in duty. The point to be emphasized before all others is that every case of affect depression is a potential suicide.

Hypomanic excitement is easily mistaken for alcoholic exhilaration. There are instances of mild manics being arrested as drunk and disorderly, although quite free from alcohol. On the other hand, the two conditions are often associated, both phases of the manic-depressive psychosis, in fact, predisposing certain individuals to alcoholic excesses.

**PARESIS AND TABOPARESIS.** Progressive, fatal disease of central nervous system following syphilis. In paresis, brain involvement and mental symptoms predominate. Speech and hand-writing defects, tremors, defective pupillary light reaction, silly euphoria, dulling of moral sense, memory defects, progressive mental decay. In tabes, cord lesions and symptoms are foremost. Defective pupillary light reaction, absent knee-jerk, ataxia, impaired sphincter control, pain crises, etc.

It is inevitable that a considerable number of enlisted men will have antecedent specific history; also that in a certain percentage the concomitant factor of personal predisposition, alcoholism, stress or what not will lead to the development of the paretic or tabetic syndrome during service.

King found general paresis to be, next to dementia precox, the most common mental disease in the army requiring institutional treatment. At the Ontario Military Hospital, Cobourg, where nervous and mental cases from the Canadian Expeditionary Forces are received, among 236 admissions of all types, 16 (6.8 per cent.) were paretics.

In other psychic disturbances likely to be encountered diagnosis rests primarily upon the mental symptom-complex. In paresis and tabes, however, three diagnostic syndromes—mental, neurological, serological—coexist and little difficulty should be experienced in a fairly early recognition of the disease.

**EPILEPSY AND EPILEPTIFORM STATES.** Despite all reasonable care in examining recruits, men with epileptic tendency will occasionally get on the strength. There are two points to emphasize:

1. There are other symptoms of epilepsy besides convulsions which may cause trouble. In cases with recurring dizzy spells, emuresis, fugue, fits of irritability or anger crises with violent acts, states of clouded consciousness and automatism with amnesia, the question of epilepsy should be considered.

2. Epileptiform seizures occur in many conditions. The chief ones are:

1. *Genuine Epilepsy*. Verified history of fits, usually from childhood; scars; character of seizures and postcritical stage; associated mental traits. Patients often report several years' free interval prior to enlistment, attacks recurring following exposure to shell fire.

2. *Post-traumatic Epilepsy*. History of old head injury followed by convulsions, with or without periods of intermission. In cases of fresh gunshot and shrapnel wounds of the skull, spasmodic motor discharges are extremely common.

3. *Hysteria*. Assuming reasonably thorough elimination of epileptics at examination of recruits, it is probable that the majority of unwounded men having convulsions will belong to the functional neurosis category. The nature and duration of attacks and independent neurotic characteristics should serve for diagnosis.

4. *Alcoholism*. Under the influence of chronic alcoholism a spasmodic diathesis may become manifest in epileptiform convulsions. The history and cessation of fits following withdrawal of the drug will clear up these cases.

5. *Parcisis*. Convulsions constitute one of the cardinal symptoms, occurring oftenest in the later course of the disease. They may appear early; occasionally, indeed, an unheralded epileptiform seizure opens the scene.

6. *Arteriosclerosis and Brain Syphilis*. Certain cases of so-called late epilepsy develop on the basis of these conditions.

7. *Brain tumor, meningitis* and other irritative lesions may give rise to epileptiform convulsions.

8. *Malingering*. Not only are the automatism and amnesia of epilepsy sometimes simulated, but even *grand mal*.

**PRIMARY MENTAL DEFECT.** Pronounced defectives have no place in the service. Higher grade morons, however, are fairly numerous in every army and many have done their bit averagingly well. It cannot be said categorically that their entire elimination on the basis of mental tests is either feasible or desirable.

Slight degrees of feeble-mindedness are easily overlooked by medical boards dealing primarily with physical conditions, but it is well to remember that inattention, forgetfulness, failure to execute orders, erratic and unreliable conduct may sometimes be traceable to this cause. Intellectual defect goes hand-in-hand with hypersuggestibility and is a suitable basis for the development of hallucinations and delusions associated with fear as well as of other neurotic or psychotic episodes.

**PSYCHOPATHIC CONSTITUTION.** This broad category includes the most difficult individuals in the army to deal with. Strictly speaking, they belong neither with the feeble-minded, the insane nor the mentally sound, yet they dwell on the confines of all three and may partake of their characteristics. Grassett puts them in the somewhat indeterminate group of "semi-insane and semiresponsible."

Constitutional psychopaths are victims of unstable or inharmonious mental development. Frequently they exhibit antisocial or criminal tendencies, pathological lying, thieving, malingering, sex delinquencies. While judgment defects in particular directions may be conspicuous, they are, in a general way, clear and rational. On the other hand,

they may possess special aptitudes, in spite of which their vacillating purpose prevents them from making a success of life; and with their usually exaggerated self-feeling they are likely to be habitually at odds with their environment. Their life history should sufficiently indicate that they will not make well-disciplined soldiers. From their ranks are recruited many of the malecontents, incorrigibles, grievance men and active trouble makers. Once the situation is recognized these men are better eliminated from the service with as little delay as possible.

**NEUROTIC REACTIONS.** *Etiology.* The psychotic and psychopathic states hitherto considered are largely independent of the military situation. Their primary causes are endogenic. Many would doubtless eventuate in the same way in civilian life. In other cases the morbid potential is accentuated under service conditions or furnishes the basis of pathological episodes which perhaps might not develop under more benign circumstances.

The neurosis, however, like all purposive conduct, is more specifically a *reaction to a given situation*. This reaction, expressing the combined effect of endogenic and exogenic factors, the war neurosis is further distinguished in the overwhelming preponderance of exogenic elements. It follows that many men will sooner or later show neurotic symptoms who might never have done so in civil life.

On the other hand, it must not be overlooked that the majority of cases develop in men *constitutionally predisposed*. In the rank and file are many men of primitive mental type, impulsive and suggestible, who are favorite victims of so-called shell shock. Not a few are high-grade defectives. They are betrayed by their naïve way of describing and explaining symptoms, particularly sensory disturbances, overlooking inconsistencies, giving variable accounts, innocently arriving at impossible conclusions.

It is generally true that the higher the type of mental organization with the implied self-discipline the less probable the occurrence of a lasting, severe, especially of a spectacular nervous disorder.

Interesting in this connection is the *difference between officers and men* in their reaction to war strain. The grosser forms of hysteria (mutism, functional paralyses, contractures, choreiform movements, ties), which are common in the ranks are extremely rare among officers.

The etiological importance of *trauma* in war neuroses has been greatly overemphasized. Its chief role may be looked for in the concussion syndrome following near-by detonation of high explosives and often accompanied by burial, the immediate effect of which is unconsciousness. This condition is discussed in another chapter. Its symptoms, like those following a blow on the head, are transitory. If enduring nervous invalidism supervenes, other causes must usually be sought than the direct effects of possible traumatism.

*Psychogenic factors* are generally conceded to be fundamental in the development and perpetuation of war neuroses. It is pertinent to refer here to the pathophilic tendency, which seems to be the inheritance of a large part of mankind. We recognize its painful development in certain individuals whose happiest recollections and favorite conversation topics are illnesses survived. Some men never outgrow the pride of childhood in crutch or sling, and to few is the derived



sympathy unpleasant. A disability may also subserve other ends. It may vouchsafe to the schoolboy a day's freedom from irksome tasks. The fact is that certain disabilities may have a motive as well as or instead of a pathological basis.

In all these respects the war disability is a thing by itself. That sooner or later "blighty" comes to be the *summum bonum* of desire is not necessarily a sign of weakness, though not all men are willing to bide their time. Hence the needless, even deliberate exposures, and occasionally self-inflicted wounds. The motive of exemption from further service must always be kept in mind. Exemption once guaranteed, the pension motive may still further complicate the situation.

Now it is a striking fact that severe physical trauma and neurosis are, as a rule, mutually exclusive. This applies especially to injuries of brain or cord. Occasional exceptions indicate that neurotics sometimes get hurt as well as other men. On the other hand, the most spectacular and obstinate symptoms of neurosis are practically confined to unwounded men. Comparable facts are familiar in civil practice.

Furthermore, severe neuroses may follow not only concussion from high explosives but also other injuries and diseases, and may develop in men who have never left camp or suffered from any definite illness or accident.

The rarity of neuroses among prisoners of war, as well as among the civilian population of long and violently bombarded districts, is noteworthy. All three classes—civilians, prisoners and combatants—may have endured similar hardships and dangers, but with the first two the fixation motive of the neurosis is lacking. Prisoners taken after exposure to shell fire often present the primary concussion syndrome; but a neurotic after-phase seldom develops.

Finally, it has been shown that neurotic conditions are relatively more frequent in hospitals distant from the front than in the field hospitals themselves. The patient removed from the atmosphere of the trenches loses the mental tone which comes from mass effort and self-suppression. Moreover, civilian, and especially home, environment, is the best possible culture medium for psychogenic disorders. Russell noted among invalided British soldiers in England the frequency of hysterical paralyses and their rarity in France.

**TYPES OF WAR NEUROSES.** In the trenches the primordial emotion of fear appears to be universal and physiological, at least as an initial or episodic mental state. Hebephrenics are reported who have sat contented and unruffled under shell fire and dauntless hypomanics may plunge with relish into the most dangerous undertakings; but probably no normal man, and few others as well, escape altogether the bitter draught of anxiety and dread.

The eventual self-adjustment is simply the net expression of the soldier's temperamental and physical qualities under such stress as he is subjected to. Obviously neurotic reactions are of all gradations from the physiological fear state, which the self-disciplined soldier masters in the performance of duty, to the paralyzing disability which totally disqualifies for further military service.

The symptoms may practically all be classified under two headings—neurasthenia and hysteria.

*War neurasthenia* shows nothing essentially distinctive. Not infrequently the constitutional nature of the condition is apparent, and aggravation occurs early during service. On the other hand, nervous as well as physical exhaustion may be considered as the accompaniment of long-endured war strain, some degree of which any man may present if he "stands the gaff" long enough. It is also significant, as Wright<sup>4</sup> has pointed out, that the majority of cases are among the older men as opposed to hysteria, which prefers youth.

Burton-Fanning<sup>5</sup> draws attention to the "predominance of neurasthenia as a cause of going sick among newly recruited soldiers" (509 cases out of 1600 hospital admissions of camp men for all causes).

The complaints of neurasthenies generally are multiple, often vague and changeable. At the same time dominant symptoms are so commonly associated with particular organs that we may conveniently speak of the group of *somatoncuroses*. In endeavoring to exclude actual organic disturbance it may be necessary to give the invalid the benefit of the doubt; but one must guard against suggesting lesions. A fixed idea of disability is sometimes traceable to an ill-advised remark by the medical examiner.

It is to be borne in mind that trophic, vasomotor and glandular changes due to influence from the sympathetic and autonomic nervous system form part of the psychogenic symptom-complex.

Somatoncurotic reactions may be: (1) *Respiratory* (dyspnea, asthmatic tendency, phthisophobia); (2) *cardiac* (symptoms described as D. A. H.—Allbutt<sup>6</sup> suggests the term "ponopalmosis" as distinguished from myocardial inefficiency following infection and other mechanical defects—n. b., thyroid, tobacco); (3) *gastro-intestinal* (anomalous abdominal pains, constipation, sometimes nervous diarrhea, introspective dieting); (4) *excretory* (usually incontinence—history of enuresis in childhood(?) retention may follow concussion, hyperidrosis); (5) *musculo-articular* (pain and weakness reactions in general, constituting the commonest neurasthenic complaints; vague histories of "rheumatism," etc., to be received with due allowance and reservation).

*Hysteria* (popularly called "shell shock") develops, as a rule, abruptly and spectacularly, and oftenest in men young in years and young in service. Of 60 cases reported by Russell<sup>7</sup> the average time spent in France was two and eight-tenths months, not all of which was at the front; 9 cases were never in France.

In the immediate pathogenesis emotional factors (anticipatory fear, horror of carnage) are preëminent, as reflected in patients' dreams. The initial symptoms are usually of a paralytic sort (universal experience following terrifying stimuli: cf. "struck dumb," "paralyzed by fear," etc.) and associated with disturbance of the higher levels of consciousness (in actual concussion, partial or complete unconsciousness). In the gradual recovery from the state of hypo- or a-function (psychic, sensory and motor) one or more functions lag behind or

<sup>4</sup> Suggestions for a Further Classification of Cases of So-called Shell Shock, Canadian Med. Assn. Jour., July, 1917.

<sup>5</sup> Neurasthenia in Soldiers of the Home Forces, Lancet, June 16, 1917.

<sup>6</sup> British Med. Jour., August 4, 1917, p. 139.

<sup>7</sup> A Study of Certain Psychogenetic Conditions among Soldiers, Canadian Med. Assn. Jour., August, 1917.

remain in abeyance (*locus minoris resistentiæ*, hysterical dissociation, perseveration of specific defence reaction against original painful stimuli or their anticipated repetition). Habit, innate pathophilic tendencies and the motive of self-advantage assist in perpetuating the morbid condition.

*Sensory Disorders.* Hysterical blindness and deafness are usually sequent to concussion and unassociated with lesions of the sense organs. Concussion symptoms begin clearing within a few hours and even an occasional ruptured tympanum should heal in due time without impairment of hearing. Mott<sup>8</sup> states that only about 17 per cent. of the cases of deafness are due, even in part, to actual ear disease. According to Hurst,<sup>9</sup> as the concussion victim regains consciousness, vision generally returns quickly, hearing shortly afterward, while the patient may remain mute for a considerable time longer. Psychogenic blindness or deafness, however, unless energetically handled, may continue indefinitely. In concussion cases, with return of sensation, painful hyperacusis or photophobia may supervene.

*Pain reactions of all kinds are regularly met with.* Cutaneous anesthesia of familiar hysterical types is not uncommon, and often accompanies functional motor disorders. The preponderance of left hemianesthesia over right holds good in war as in peace, most soldiers, like most civilians, being right-handed.

*Motor disorders* of psychogenic origin include derangement of the speech mechanism (mutism, aphonia, dysarthria, dysphasia, stammering, even motor aphasia); ties (usually of head or face; general trembling (to the degree of making walking, even standing unsupported, difficult or impossible); tremor of extremities, worse under observation, even suggesting intention tremor; choreiform movements; myoclonus; epileptiform convulsions; rhythmic movements; local pareses, paralyses and contractures of all description.

Increased psychomotor irritability, with hypertonic and hyperkinetic symptoms, is by far the commonest disturbance of motility. Even in convalescents of many months a sudden, unexpected auditory or touch stimulus may produce a violent motor discharge with incoordinated spasmodic movements.

A special type of functional contracture is trench spine, the lineal descendant of railway spine. It varies from moderate rigidity of the back muscles, with complaint of pain to a maintained right-angle kyphosis ("camptocormie" of French writers),<sup>10</sup> the invalid walking like a carpenter's square on end. Various other antipain postures occur, as well as perseveration limps, even conspicuous apparent shortening of one leg through tilting of the pelvis.

*Psychic Disturbances.* In concussion cases a stuporous state may persist for several days, furnishing the cue for continuing individual symptoms (*e. g.*, amnesia) and episodic conditions such as dream-waking, hallucinations (sounds of battle), automatism.

Concussion amnesia is a matter of hours. Psychogenic amnesia may cover a much longer period both anterograde and retrograde.

<sup>8</sup> Mental Hygiene and Shell Shock during and after the War, British Med. Jour., July 14, 1917.

<sup>9</sup> Medical Diseases of the War, Arnold, London, 1917, p. 9.

<sup>10</sup> Souques and Rosanoff-Saloff: Rev. Neurol., November and December, 1915

Oppenheim,<sup>11</sup> comparing cases of trephine amnesia with those following shell shock without external injury, found the latter much less likely to retain memories of their trade or profession than the former.

One man returned from the front maintained total inability to recall anything in his past life, including his marriage, the appearance of members of his family, the streets of his native town. He dated contemporary recollection from a shock received when in a fit of agitation he left his bed and dashing through the ward collided with a brick wall.

Loss of memory is a favorite complaint of war neurotics, but coöperation is not always of the sort to make memory tests of value.

Many patients display a degree of mental sluggishness and lack of initiative with unapparent will to recover. They are mildly bored as they recount the various kinds of treatment their infirmity has successfully withstood. In others the dominant characteristic is a childish timorousness, with emotional instability, tearfulness and painful loss of self-confidence. Soldiers, like horses, may become broken-spirited.

Not infrequently there is observed in the psychic sphere a condition suggestively analogous to postconcussion asthenopia due to defective innervation of the ciliary muscles. There is definite retardation, varying with the difficulty or affective content of the response, and particularly an insufficient fixation and maintenance of attention, the patient tending to lapse into silence, with apparent diffusion of attention. Such an individual placed in new surroundings does not readily assimilate the usual data of orientation and easily loses his way.

In connection with the war neuroses it is to be noted that transitory conditions suggestive of severe psychoses are much commoner than in civilian practice. Under field conditions, for example, a permanent schizophrenic process may first come to light, partially masked perhaps by reactive neurotic symptoms. On the other hand, a soldier with mild schizophrenic traits may under war stress or during the course of a neurosis pass through an acute psychotic episode which clears up rapidly and which might not have occurred in ordinary life.

In dealing with the war neuroses in general one repeatedly encounters the difficulty of avoiding the inference, however slight, of some element of deception. But this feature should always be first a matter of clinical rather than ethical judgment. Major Russell,<sup>12</sup> on the basis of his exceptional experience at Granville Special Hospital, divides all nervous disturbances without corresponding signs of organic disease into two categories: (a) hysteria; (b) malingering. This classification involves a dilemma both horns of which may be unpleasantly pointed. Russell steers safely between by promptly discarding his classification and applying the term "psychogenetic condition" to everything in both groups. This "does away with the necessity of making a distinction between those cases which may be suspected of voluntary simulation of symptoms and those others which are genuine."

*Treatment.* Cases of neurosis should be turned over with as little delay as possible to psychiatric units or special hospitals. Their successful management depends more upon the personality, acumen

<sup>11</sup> Traumatic Amnesia, *Prog. méd.*, Paris, June 2, 1917.

<sup>12</sup> *Loc. cit.*

and assurance of the medical officer than upon any pet method he may invent or follow. The great variety of measures in vogue indicates that the war neuroses do not differ in this respect from those of everyday life. Only certain guiding principles need here be referred to.

Treatment should be started promptly and carried out rapidly and determinedly. There should be as little relaxation of military discipline as possible. Men do better, as a rule, in the atmosphere of the war zone than when far removed, especially to their home districts. Visits and communications from relatives and friends are often contra-indicated, and it is questionable policy to allow a neurotic invalid home on pass before or during treatment.<sup>13</sup>

For certain shock symptoms a counter-shock may be all that is required. One "postconcussion" mute suddenly regained the power of speech when the stretcher-bearers accidentally dropped him. Victims of painful stammering sometimes show remarkable ease and fluency of utterance when anger-provoking stimuli lead to an outburst of profanity.

Intensive, even heroic, procedures are best adapted to the more spectacular motor and sensory disorders;<sup>14</sup> although in some instances the mere knowledge, on the part of the patient that a certain object upon which he has set his heart can only be attained after a perverted or suspended function has returned to normal, may bring the desired result.

Treatment of the neuroses includes not only active measures to overcome disabling symptoms, together with tonic, nutritional, rest and sedative agencies, electro-hydro-therapeutics, etc., as indicated in individual cases, but also a certain amount of psychomotor reëducation. A new mental attitude and a new way of self-management should be aimed at to ensure the after-condition of the nervous invalid. The end of the war will automatically bring many self-adjustments and cures, but an expectant method based on this contingency is hardly justified.

Congenital and systematic occupation should be given foremost place in any scheme of treatment. Idleness and moving about from hospital to hospital should be reduced to the uttermost minimum. Charcot said: "*Il ne faut pas laisser flâner les contractures hystériques.*" This golden rule applies to all war neurotics. The best preventive for the terrifying dreams which are so common is, as Russell points out, regular and interesting work.

Prophylaxis begins with the selection of recruits. After work in camp a period of training behind the lines is the method best calculated to reduce the danger of nervous break-down. It has been suggested that the depressing after-effects of alcohol issued to men about to go into action may heighten the susceptibility of the nervous system to neurotic reactions. The possibility is worth considering.

<sup>13</sup> Every rule has its exception. A speechless soldier, out on pass, got drunk with some friends and in the cheeriness of the occasion recovered his voice.

<sup>14</sup> Sir William Osler calls the precipitate and successful methods in use in the Granville Hospital "therapeutic jugulation." As might be expected, Germany was not slow in devising heroic means of treatment. The "Ueberrumpelung" method with severe and painful electric stimuli has resulted in cures, and has also been followed by deaths.

Finally, it would seem highly desirable to incorporate in the system of training a certain amount of information concerning war neuroses and to teach mental hygiene as well as physical. Morton Prince<sup>15</sup> has already put this suggestion into tangible form.

There has come into being at the front—nor is it confined to the front, nor yet to the army—a shell-shock tradition which should be combated by all available means. This tradition implies an actual physical injury to the nervous system as cause and some sort of severe organic disability as the result. Moreover, it makes shell shock the disease of the hour, so to speak—a disease not only new, but by association preëminently distinguished. There might be fewer and shorter cases if Prince's term "shell funk" were officially substituted for the more impressive and euphonious "shell shock."

### ORGANIZATION AND ACTIVITIES OF THE AMERICAN RED CROSS BUREAU OF SANITARY SERVICE.

JANUARY 10, 1918.

TO ALL DIVISION MANAGERS, AMERICAN RED CROSS:

In accordance with an agreement reached at the meeting of the American Red Cross Division Managers, held at Washington, D. C., January 8 and 9, 1918, I transmit herewith a synopsis of the activities of the Bureau of Sanitary Service, American Red Cross.

(Signed)

J. CLARK,

Surgeon, U. S. Public Health Service,

Acting Director, Red Cross, Bureau of Sanitary Service.

On June 14, 1917, a "Memorandum Relative to Coöperation of the Red Cross with the United States Public Health Service in Sanitary Matters Having an Effect on the Prosecution of the War" was presented to the Medical Advisory Committee of the War Council and approved:

The Bureau of Sanitary Service, to operate under the Department of Military Relief, was established by resolution of the War Council of the American Red Cross July 17, 1917, and a provisional appropriation of \$10,000 was authorized for its organization and development.

The primary object of the American Red Cross in establishing the Bureau of Sanitary Service was for the purpose of giving aid to Federal, State and local authorities in securing and maintaining effective sanitary control in the civil districts surrounding or adjacent to National Army Cantonments, National Guard Camps and Naval Bases.

The control of sanitary matters in the civil districts adjacent to the various military areas is a function delegated by legislative enactment to State health authorities, and through them to local health organizations. State and local funds for such purposes in the past have been extremely limited, a condition that can be remedied only by legislative action, a procedure requiring a considerable period of time to accomplish.

<sup>15</sup> Jour. Am. Med. Assn., September 1, 1917.

The relatively rapid mobilization of troops in certain areas accompanied by almost equally sudden and great increase in the civilian population in the vicinity of the selected camp sites, created new conditions and increased the necessity for more rigid sanitary control in extra-cantonment areas, an emergency that would tax the resources of the best health organization to meet. The local health authorities were therefore forced in nearly every instance to call on State or Federal authorities for assistance.

The United States Public Health Service, by law, is empowered to cooperate with State and local authorities in the prevention and control of communicable diseases, and had already taken steps to assist these authorities. In view of the limited personnel and available funds and, furthermore, because of the necessity for speedy action in affecting the sanitary control of extra-cantonment areas, it seemed warranted for the American Red Cross, supported largely by contributions from the whole people, to cooperate with Federal, State and local authorities in this national emergency. The Bureau of Sanitary Service, therefore, was established and Surgeon W. H. Frost was detailed by the Surgeon-General of the United States Public Health Service to act as the director. Unfortunately, Surgeon Frost was forced to relinquish this position by reason of ill health, and resigned the directorship on November 6, 1917.

*Organization of Sanitary Units.* Under a broad plan of cooperation between Federal, State and local health authorities and the American Red Cross, the Bureau of Sanitary Service is furnishing personnel and funds to complete the sanitary organizations in extra-cantonment areas, supplementing the resources of the local communities, the State and the Public Health Service until some provision can be made for supporting these organizations without the aid of the Red Cross. Assistance is given by the Red Cross only upon request from local or State authorities on recommendation of the Surgeon-General of the the Public Health Service, based upon a preliminary survey in the vicinity of each cantonment to determine whether the conditions in the district establish the need for aid.

The Red Cross furnishes supplementary assistance by assigning to the district a group of trained assistants, bacteriologists, sanitary inspectors, Red Cross public health nurses, with an appropriation sufficient to provide the necessary equipment, transportation and maintenance, which group is organized into a Red Cross Sanitary Unit.

The cooperative health organizations thus established represent the combined resources of Federal, State and local authorities supplemented by auxiliary assistance from the Red Cross. The administration of its activities is placed under the direction of the public health officer who acts also as director of the Red Cross Sanitary Unit. To him State authorities delegate the power and authority of deputy State health officer and all activities are coordinated and centralized under his supervision.

An Officer of the Public Health Service, or one recommended by that service, is appointed director of the unit and is immediately responsible for the work.

Associated with the director of the unit is a fiscal officer, usually a

local business man appointed on the recommendation of the local Red Cross Chapter, who is the fiscal agent responsible for the funds appropriated.

Places to which sanitary units have already been assigned:

Unit No. 1.	Columbia, S. C.	Unit No. 14.	Macon, Ga.
2.	Little Rock, Ark.	15.	Manhattan, Kan.
3.	Louisville, Ky.	16.	Chattanooga, Tenn.
4.	Des Moines, Iowa	17.	Spartanburg, S. C.
5.	Leavenworth, Kan.	18.	American Lake, Wash.
6.	Hattiesburg, Miss.	19.	Montgomery, Ala.
7.	Petersburg, Va.	20.	Charlotte, N. C.
8.	Anniston, Ala.	21.	Waco, Texas
9.	Newport News, Va.	22.	Alexandria, La.
10.	Ayer, Mass.	23.	Fort Worth, Texas
11.	Atlanta, Ga.	24.	Wrightstown, N. J.
12.	Chillicothe, Ohio	25.	Augusta, Ga.
13.	Greenville, S. C.	26.	San Antonio, Texas

The personnel of the 26 units is as follows:

Directors (services free) . . . . .	26
Assistant directors (service free) . . . . .	17
Fiscal officers (services free) . . . . .	26
Assistant fiscal officers (services free) . . . . .	20
Bacteriologists (paid employees) . . . . .	6
Minor employees (paid employees) . . . . .	5
Sanitary inspectors (paid employees) . . . . .	52
Red Cross Nurses (paid employees) . . . . .	51
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*Transportation.* Under the authority voted by the War Council, August 24, 1917, Ford automobiles have been allotted in requisite number, usually two, to the respective sanitary units for use by inspectors and nurses in the territory adjacent to military encampments.

*The Work of the Sanitary Units.* The work of these local organizations in which the Red Cross unit coöperates is also varied to meet conditions, but in general it includes the following: A public health laboratory, in charge of a competent bacteriologist established for bacteriological examinations of water and milk supplies and to assist in the diagnosis of infectious diseases. A house-to-house inspection of sanitary conditions is made in the whole district. Insanitary conditions must be remedied by the property owners, after which regular inspections must be made at frequent intervals. Systematic inspection is established for dairies, milk depots, restaurants, markets and all places where food and refreshments are prepared or sold. Special effort is made to have all cases of infectious diseases promptly reported and to have each case, as reported, visited by an inspector or a public health nurse to instruct the attendants in necessary prophylactic measures and to see that they are carried out.

*Prevention of Malaria.* Special work is necessary in most Southern districts for the prevention of malaria. This requires the eradication of malaria-bearing mosquitoes in a fairly wide zone surrounding the cantonment, and also the adjacent centers of population which are visited frequently by men from the encampment. The work of



mosquito eradication is not confined to communities in which malaria is highly prevalent. It is being carried out in all the districts where malaria mosquitoes are found in considerable numbers, and when there is a possibility that malaria might become more prevalent with the increase of population due to the establishment of the camp.

The same principle applies to other sanitary work, and the fact that active sanitary measures are undertaken in the vicinity of a camp does not necessarily mean that previous sanitary conditions in that district were especially bad.

*Isolation Hospitals.* The question of isolation hospitals for the segregation and treatment of communicable diseases has been given consideration. The War Council appropriated on August 14, 1917, \$1000 to be used in the study of this project. Dr. Charles V. Chapin, Superintendent of Health of Providence, R. I., a member of the Medical Advisory Board and a prominent sanitarian, upon request, visited several cantonment areas. In his report he questioned the advisability of the expenditures necessary for the purchase of portable hospital units. He concluded that the chief requirement would be a good organization for the control of contagious diseases in each area.

The effective control of ordinary communicable diseases in extracantonment areas seems, largely, to depend upon the efficiency of the cooperative health machinery established.

*Auxiliary Nursing Service.* Steps have also been taken to inaugurate an auxiliary nursing personnel to be available in case of epidemics or other emergency.

*Mobile Laboratory Cars.* Four mobile laboratory cars authorized by the War Council August 14, 1917, are now in commission. Wooden Pullman cars have been converted for this purpose and all necessary apparatus has been installed in two of these cars, including sleeping quarters for a maximum personnel of ten workers and assistants.

These cars, when in active service, will be operated by volunteer professional men, skilled in the diagnosis and treatment of diseases. Ordinarily a professional staff of about five men will accompany each car when in service. In addition, provision has been made for the services of cooks, technicians and a fiscal officer.

Upon a written request from the Surgeon-Generals of the Army, Navy or Public Health Service the nearest available car with personnel and equipment will be dispatched to a designated point with instructions to the director to confer with the proper local authorities. They are based under designation at the following places:

"Lister," Director Dr. L. Hektoen, Chicago, Ill.

"Metchnikoff," Director Dr. Fred P. Gay, San Francisco, Cal.

"Pasteur," Director Dr. James W. Jobling, Nashville, Tenn.

"Reed," Surgeon-General, U. S. Army, Washington, D. C.

The "Pasteur" was detailed December 5, 1917, to assist the personnel of the base hospital at Camp Bowie, Fort Worth, Texas, in pneumonia work and has just been requested for service at Camp Beauregard, Alexandria, La., in meningitis work. The car "Lister" was similarly detailed December 27, 1917, to Camp Doniphan, Fort Sill, Oklahoma. All of these details were made on request of the Surgeon-General of the United States Army. On request, with the approval

of the Director-General of Military Relief, January 3, 1918, the car "Reed" has been placed in custody of the Surgeon-General of the United States Army, to be operated and manned by a staff from the Medical Corps of the United States Army.

*Venereal Disease Control.* Under the authority of resolution by the War Council, November 14, 1917, making appropriation to be expended by the Director of the Bureau of Sanitary Service for coöperation with the Army and Navy, Public Health Service and with State and local health authorities in the control of dangerous communicable diseases, nine clinics for the treatment of "carriers" of venereal infection have been established and funds set aside for their maintenance for the protection of military forces in extra-military areas. It is proposed to establish other clinics as rapidly as practicable, in accordance with the following plan:

1. Inasmuch as the venereal diseases are only a part of the general problem of communicable diseases for the control of which the United States Public Health Service has assigned officers as directors of sanitation in each of the extra-continent areas, and has already taken steps for the treatment of "carriers" and the hospitalization of certain cases, it is proposed that the local administration of whatever measures are instituted for the control of these diseases shall be by the directors of sanitation in the areas in question.

2. For the purpose of selecting the best measures for the control of venereal diseases, there shall be established, at first, dispensaries or clinics for such diseases in only a few selected areas.

3. The function of such a clinic shall be (a) treating "carriers" of venereal infection; (b) hospitalization of selected cases wherever practicable; (c) utilizing and instructing local practitioners in the control of venereal diseases; (d) distributing, free of cost, to local practitioners, salvarsan and other venereal remedies under prescribed regulations; (e) making free bacteriological examinations, serological tests and other laboratory investigations of venereal diseases at the request of local practitioners and certain administrative officers; (f) advising persons who may desire confidential information, with respect to possible infection of themselves, proper treatment and related subjects.

4. It is proposed that the existing sanitary units in the selected areas shall be supplemented by the following personnel:

- One specialist in venereal diseases.

- One or two probation officers.

- One social worker.

- One clinic nurse (male).

- One clinic and follow-up nurse (female).

- One to four policewomen.

5. It is proposed that the United States Public Health Service provide and pay the salary of a general specialist for each established clinic wherever the services of such a specialist shall be required.

6. It is proposed that the United States Army, through the Commission of Training Camp Activities, provide the necessary probation officers to study and act upon individual cases, secure the necessary attendance at clinics and for such other additional duties as may arise in connection with persons convicted in the local courts who may be suffering from venereal infection.

7. It is proposed that the United States Army will continue the services of a social worker in such extra-cantonment areas for educational and other purposes.

8. It is proposed that the American Red Cross shall furnish one male nurse for clinic purposes and one female nurse for combined duty in the clinic and follow-up work.

9. It is proposed that the necessary surgical appliance and drugs shall be provided by the American Red Cross in the amounts needed.

10. It is proposed that the American Red Cross shall furnish the necessary transportation for follow-up work and other control measures in connection with these clinics.

11. It is proposed that the providing of proper office space shall be requested of the local authorities. In the event of the inability of the local authorities to provide such quarters, the same shall be provided from appropriations of the American Red Cross.

12. It is proposed that a requisite number of policewomen shall be furnished by the local authorities to properly enforce anti-prostitution ordinance.

13. It is recommended that clinics so established shall be continued for a provisional period of six months, and longer should the necessity of the work warrant such procedure.

14. The United States Public Health Service is prepared to make the necessary bacteriological examination, serological tests and other laboratory investigations.

15. It is proposed that pamphlets on the control of the venereal diseases and other educational material shall be requested of the American Social Hygiene Association for free distribution.

*Public Health Nursing.* A supervising public health nurse recommended by the Bureau of Nursing Service has been appointed by the Public Health Service. This nurse will assist the extra-military areas where sanitary organizations have been established and also study public-health nursing requirements. This supervision, direction and development of nursing activities will be extended to all nurses employed under the central health organization.

*Inspection of Red Cross Sanitary Units.* The Surgeon-General of the Public Health Service has detailed an officer of that service to visit and inspect all Red Cross Sanitary Units. This officer will be expected to remain at each unit a sufficient length of time to familiarize himself with the operations of the unit, and upon the completion of his investigations to submit a written report with such recommendations as seem necessary for increasing the working efficiency of the unit.

## REVIEWS

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DISEASES OF THE NERVOUS SYSTEM. By SMITH ELY JELLIFFE, M.D., Ph.D., and WILLIAM A. WHITE, M.D. Second edition, revised, rewritten and enlarged. Pp. 938; 124 engravings and 11 plates. Philadelphia and New York: Lea & Febiger, 1917.

THIS is the second edition, the first having been reviewed in this JOURNAL some years ago. The present edition has been considerably enlarged, there being added a general introduction setting forth the purpose of the volume. The chapters on the vegetative nervous system and the endocrinopathies have been entirely rewritten. Advantage has been taken of the war literature, and such additions can be found in the chapters on injuries of the peripheral nerves and of the brain. Otherwise the book remains the same. There is no question that the organic part of this work is excellent. The authors know what they are talking about and their method of presentation is direct and to the point. Their presentation of organic anatomy and physiology and the symptoms of organic nervous diseases is excellent, although they have not taken advantage of the recent literature on cerebellar disease, and the whole discussion of cerebellar symptomatology is old. The presentation of the vegetative nervous system and of the functions of the internal glands is the best that can be found in any text-book on nervous diseases; in fact, there is no text-book on the nervous system which covers this point so fully and as well as this. The illustrations are very good and are well chosen. Most of them are from the French, after Dejerine. They are perhaps the best in existence, and the authors have done well in choosing them.

Both authors are well known as disciples of Freud, and have popularized Freud's teachings perhaps more than anyone else in this country. Their conception of the neuroses is entirely Freudian, and they have no patience with the older view-point. In fact, they do not mention it. The large amount of literature on shell shock is not discussed, excepting that shell shock is mentioned in the discussion of traumatic neuroses, and it is noted that shell shock develops in those with a psychopathic constitution. The presumption is that the authors regard shell shock from the Freudian stand-point. The psychiatric portion of the work is excellent, and of course is from the Freudian view-point.

T. H. W.

MODERN DIETETICS. By LULA GRAVES, Dietitian, Lakeside Hospital, Cleveland. Pp. 202. St. Louis: The Modern Hospital Publishing Company, 1917.

THIS monograph, representing a collection of eight papers on "Feeding the Hospital," recently published in the *Modern Hospital*, has very justly received much popularity.

It is especially valuable to dietitians, hospital officials, physicians, medical students and nurses—as well as to institutional, government and military officials.

Good foodstuffs, intelligently selected, properly stored, prepared and served by experienced persons are economic essentials.

Food composition and the body's need and use of food is carefully explained. Each class of food is discussed as to its characteristic composition and food value, and its place in the dietary.

Special diet for use in disease, in various different institutions and in different classes of people are outlined, with complete recipes for both institution and home use. The composition and caloric value of each recipe is given and the Atwater tables are attached.

Especially interesting and most complete are the suggestions as to training-school work in dietetics, making the book a valuable one to domestic science classes.

The book is well written and of more value to institutions than to private homes.

J. D.

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A MANUAL OF ANATOMY. By HENRY ERDMANN RADASCH, M.Sc., M.D., Assistant Professor of Histology and Embryology in the Jefferson Medical College, Philadelphia. Philadelphia: W. B. Saunders Company, 1917.

THE desirableness of placing in the hands of the preparatory or the first-year medical student a reliable volume of modest size, anticipating the study of the elaborate text-books of anatomy, is widely recognized. The preparation of a manual meeting these requirements was the task that Dr. Radasch has undertaken, and very acceptably completed, since within the 473 pages of the book is contained an up-to-date account of all the more important structures of the human body.

The author has been fortunate in being able to utilize the admirable plates of the well-known *Atlas* of Sobotta-McMurrich as the illustrations for his book, either as direct reproductions, or as the basis of simplified line drawings. In addition a number of original sketches and diagrams, as well as photographs, are included in the 329 figures elucidating the text.

In adopting the BNA names the author has decided wisely, since the use and demand for this terminology is steadily increasing.

The misnomer, "false," as applied to certain vertebræ and ribs should be eliminated, conveying to the student, as it does, erroneous notions as to morphological values. In places the names appearing in the text do not agree with those of the legends of the figures. Thus, although the illustrations of the hip bone are labeled innominate bone, no mention of the term occurs in the text—a discrepancy making for the confusion of the student.

The series of excellent diagrammatic drawings, showing the course of the lymph paths and the position of the nodes, is a valuable feature of the book. The section devoted to the central nervous system is adequate and contains many instructive diagrams. The retention of the now obsolete name corpora albicantia for the corpora mammillaria is odd in a book avowedly adopting the new terminology. Labeling (Fig. 279) the gyrus einguli as the "eingulum," one of the association tracts, is misleading. But these are minor shortcomings that may easily be corrected in later editions; on the whole, Dr. Radasch has surely earned the gratitude of the group of students for whom the book was written.

G. A. P.

COLLECTED PAPERS OF THE MAYO CLINIC, ROCHESTER, MINN.  
 Edited by MRS. M. H. MELLISH. Volume VIII, 1916. Pp. 1014;  
 411 illustrations. Philadelphia and London: W. B. Saunders  
 Company, 1917.

THIS large volume, containing publications by the staff of the Mayo Clinic during 1916, is made up of 93 separate articles from 42 authors, and it is explained in the foreword that several of these are presented only in abstract and that others are held over for subsequent publication. The greatest number of papers are from the pen of Dr. Charles H. Mayo, who contributed ten, no other member of the staff having produced during that year more than five. The average of more than two papers for each writer is an enviable record, and cannot be equalled by many teaching or research institutions.

While most of the publications deal with practical surgical problems, there are many that emanate from the laboratories, and that have a bearing upon medical as well as surgical conditions. The contents are arranged according to systems under the following headings: alimentary canal, urogenital organs, ductless glands, blood, and head, trunk, and extremities. There is another group of articles dealing with technique, in which are described a water-cooled retractor for use in the mouth, staining methods for use in the study of pathological lesions in sympathetic ganglia, and a very clever machine for shaking blood-mixing pipets. The final section contains general matter, such as the element of error in abdominal

diagnosis, an appreciation of the roentgen rays, hospital problems of gonorrhea and syphilis, the value of public health service, the status of the graduate degree in medicine, and an able appreciation by Dr. William J. Mayo of Dr. John B. Murphy.

The illustrations deserve special mention, being in every instance well done; this is in part attributable to the excellent grade of paper employed by the publishers, but particularly to the care with which the specimens, apparatus, models, etc., have been prepared and photographed. An index of contributors, a bibliographical index, and an index of subjects, the latter covering 19 pages, concludes this valuable 1916 contribution from the Mayo Clinic. T. G. M.

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ERFAHRUNGEN ÜBER DIAGNOSTIK UND KLINIK DER HERZKLAPPENFEHLER. By PROFESSOR S. E. HENSCHEN, chem. Direktor der medizinischen Universitätsklinik in Upsala und der medizinischen Klinik in Stockholm. Pp. 355. Berlin: Julius Springer.

In this exhaustive study of 300 cases of valvular heart disease, the author takes up the subject from almost every point of view. The case protocols are given in considerable detail and the individual valve lesions are grouped together. Considerable space is devoted to certain combinations of valvular lesions which are clinically seldom seen and are of little clinical importance. In the latter part of the volume there is a lengthy discussion of pulse curves with many radial pulse tracings. These are unaccompanied by jugular tracings and so must depend in many instances for their value on the character of the curves, a point of doubtful value. No electrocardiographic curves are given. On the whole the work is lengthy, undigested, and presents nothing new. O. H. P. P.

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A CHEMICAL SIGN OF LIFE. By SHIRO TASHIRO. Pp. 142. Chicago: The University of Chicago Press, 1917.

THIS is a very interesting little book. The preface, part of which is quoted, gives an adequate idea of the purposes of this work:

"The present work is an attempt to apply facts discovered during the study of the physiology of nerves to living processes in general. That mechanism characteristic of all living matter which enables it to respond to the external world is best developed in the nervous system. This mechanism may be called the most characteristic thing in life. The chemical accompaniment, or basis, of this mechanism, discovered by the author in nerve fibers, he has hoped

to show exists also in all forms of living matter, both of plants and of animals. It gives a chemical method of distinguishing living from dead tissue, and of measuring the quantity of life.

"This book therefore contains somewhat in detail all the essential facts which he with his students has discovered from studies of the chemical changes in nerves accompanying functional change. In the presentation of this work, however, many important references and discussions have been omitted in order that the reader may not lose the main trend of the argument. The facts themselves are nevertheless given in the form of accurate numerical data so that the book may be useful also to the specialist whose interest lies more directly in the general physiology of the nervous system."

According to the author there are two signs or tests which all living things show and which are an index of life. One of these is an electrical disturbance, discovered one hundred years ago, and the other a chemical sign, just discovered and discussed in this book. According to the author's experiments it has been shown that the living nerve fiber is no exception to the rule that all living matter undergoes chemical changes. This is shown by means of a biometer invented by the writer. By the use of this apparatus the author showed that the living nerve fiber normally gives up a certain amount of carbon dioxide and that when it is excited the amount of carbon dioxide is increased. Dead or anesthetized nerves show no such change. This discovery is applied to the practical question of finding out whether or not a seed is dead or alive. This work is very interesting and is full of suggestions for the future. T. H. W.

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THE PRINCIPLES OF GYNECOLOGY. By W. BLAIR BELL, B.S., M.D. (Lond.), Gynecological Surgeon, Royal Infirmary, Liverpool. Second edition. Pp. 523; 363 illustrations and 6 colored plates. New York: William Wood & Co., 1917.

SEVEN years have elapsed since the first edition of this book was presented to the medical profession, but aside from minor alterations in the text and some improved illustrations the book remains much the same. The peculiar arrangement of the subject matter under pathological headings rather than the classification of the various disease entities according to the organs involved, greatly dismembers the continuity of many of the subjects and detracts from the value of the work as a working guide for the student.

The description of the operative procedures that are employed in gynecological practice is very brief, as perhaps it should be in a work of this kind, while on the other hand, considerable attention is paid to detail in the description of minor gynecological practices, as, for example, the pessary treatment of retroversion of the uterus.



References to the work of others and conflicting opinions of authoritative gynecologists are purposely excluded since the author merely desires to present his own observations and experiences. This feature, together with the inclusion of chapters on venereal diseases, obstetric problems and electrotherapy in gynecology should make the book especially interesting to the general practitioner.

F. B. B.

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THREE CONTRIBUTIONS TO THE THEORY OF SEX. By PROF. SIGMUND FREUD, Vienna. Authorized Translation by A. A. BRILL, M.D. Nervous and Mental Disease Monograph Series No. 7. Pp. 116. New York: Nervous and Mental Disease Publishing Co.

THIS is the second revised and enlarged edition of this work, which appeared some years ago. The present edition has an introductory chapter by James J. Putnam. According to him the keynote of psychoanalysis is in the understanding of the sex instinct and its development. This work, of which this is an excellent translation, presents the essential views of Freud on this subject. No understanding of psychoanalysis is possible unless one understands the theory of sex, and there is no better presentation in the English language than this.

T. H. W.

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DISEASES OF WOMEN. By HARRY STURGEON CROSSEN, M.D., F.A.C.S., Associate in Gynecology, Washington University Medical School. Fourth edition, revised and enlarged. Pp. 1125; 800 illustrations. St. Louis: C. V. Mosby Company, 1917.

THE appearance of a fourth edition of this book within ten years from the date of the initial edition is, of itself, sufficient to prove that it has met the requirements of the medical profession. It would hardly be fair to the author, however, if the merits of the book were passed by with such a simple statement of fact. The character and scope of this work are such that it has always been considered among the best books of its kind, and the present edition, enlarged and revised, has been brought right up to the minute as evidenced by the careful consideration of such subjects as the radium treatment of inoperable cancer of the uterus and fibroid tumors.

A large part of the credit for the present revision is due to the painstaking care of Dr. Hugo Ehrenfest, who relieved Dr. Crossen of this difficult task when the latter was called to military duty, and especially must mention be made and due credit given to Dr. Ehrenfest for the excellent chapter which treats of the relation of the

ductless glands to the female generative organs. No present-day volume of this character can be considered complete without a thorough presentation of the present status of the endocrine organs and organotherapy, and in this field, as indeed throughout the entire book, the author has left out nothing of importance.

Owing to the fact that little material is deleted with the appearance of successive editions, the present volume has reached quite a large size and is more profusely illustrated than any of its predecessors. The illustrations consist chiefly of semidiagrammatic drawings, photomicrographs and photographs of patients and specimens, all well selected. There should be no hesitancy in venturing the opinion that this work will continue to enjoy the popularity that it has long since attained.

F. B. B.

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A MANUAL OF NERVOUS DISEASES. By IRVING J. SPEAR, M.D.  
Pp. 660; 172 illustrations. Philadelphia and London: W. B. Saunders Company.

THIS volume is intended for the student and for the general practitioner. It is a little larger than a compend, containing quite fullsome descriptions of the anatomy and physiology of the nervous system and of the different organic and functional nervous conditions. There is nothing original about the book, it following along the old and well-known lines. It has apparently been carefully compiled, but it can hardly be said to be up to date. For example, according to the author the motor centers are not only in the precentral convolutions but in the anterior portion of the post-central, whereas for many years everyone has agreed that they are entirely located in the precentral convolution. For the cerebellum no attempt is made to give modern localization, and the author states that disturbance in the middle lobe may cause forced movements, tremors, and cataleptic attitudes, and that disease of the cerebellum may bring about incoördination, abnormalities of movements, ataxia, vertigo, speech disturbance, nystagmus, adiadochokinesis, disturbances of equilibrium, etc. In other words, a repetition of all of the symptoms that the cerebellum has been accused of for years, whereas it can all be very well summed up in one word, "disturbances of synergy." In discussing the symptoms of locomotor ataxia the author states that the tendo Achilles reflex is rarely absent and that the reflexes of the upper extremities are generally preserved and are often increased; whereas everyone knows that the tendo Achilles-jerk is just as frequently absent as the knee-jerk, and that it is only in rare instances that the upper arm reflexes are preserved. In discussing tumors of the brain, he states that gliomatous tumors are third in frequency, whereas all path-

ologists state that it is the most common. These are only instances of inaccuracies which are found throughout the book. Such inaccuracies have no business to occur in any modern book on the nervous system.

T. H. W.

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INFECTED WOUNDS. By A. CARREL and G. DEHELLY Pp. 238; 97 illustrations. New York: Paul B. Hoeber, 1917.

THIS little treatise has been translated by Herbert Child, and has an introduction by Sir Anthony A. Bowlby, Surgeon-General to the British Armies in France, whose sanction it carries. The book takes up the treatment of wounds in every phase, and tries to show that antiseptics, especially the chlorine group, can be relied upon to do almost phenomenal work. The principles of the technic of the Carrel-Dakin treatment are clearly elaborated, the technic of the making of Dakin's solution, the sterilization of wounds, mechanical, chemical and surgical sterilization, the bacteriological examination and the final closure of the wound are all described in the most extensive manner.

The book is remarkable for the detail and the minutiae of its varied descriptions.

The reader must, however, bear in mind that the primary treatment demanded by wounds is good surgery and its associated clinical care. These, coupled with antiseptics well applied and intelligently used will usually give good results.

The book rather emphasizes the antiseptic treatment and its value, more than the surgical management of wounds.

The results claimed are almost phenomenal. E. L. E.

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THE HISTORY OF THE PSYCHO-ANALYTIC MOVEMENT. By PROF. DR. SIGMUND FREUD, Vienna. Nervous and Mental Disease Monograph Series No. 25. Authorized English Translation by A. A. BRILL. Pp. 58. New York: Nervous and Mental Disease Publishing Company, 1917.

THIS is another of the Nervous and Mental Disease monographs, and is a very interesting contribution by Freud himself on the history of the psycho-analytic movement. The translation is by A. A. Brill. It contains Freud's own history of the movement, and as such is interesting from the psycho-analytic stand-point. The last part of the paper is a protest, or rather a discussion, of the modifications of psycho-analysis by Adler and Jung. Freud concludes that Jung's new theory, which he desires to substitute for psycho-analysis, emphasizes an abandonment of analysis and a cessation from it.

T. H. W.

# PROGRESS OF MEDICAL SCIENCE

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## SURGERY

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UNDER THE CHARGE OF

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**Course and Treatment of Joint Suppurations; the Technic of Making the Drainage Opening.**—PAYR (*Deutsch. Ztschr. f. Chir.*, exxxix, 1) discusses this subject from the stand-point of his military service and lays particular stress on the various routes for opening the different joints for drainage, using numerous excellent illustrations for these operations. The following methods of treatment were employed: Tincture of iodine, Lugol's solution, or phenol-camphor, was injected into the joint. The last substance is to be employed only when there is not a large effusion in the joint. Otherwise carbolic acid would appear in the urine. It is not to be employed in hemarthroses, because it increases the clot formation which interferes with later punctures. This method should be employed in the treatment of beginning infection and particularly for the prevention of threatening joint infection. We may employ puncture with a trochar, pressing out and aspiration of the blood exudate; irrigation of the joint with a 0.5 to 1 per cent. carbolic solution or a weak Lugol solution, of which a little should be left in the joint. Adhesion formation is not to be feared in these cases of acute infection. This method is to be used in serofibrinous effusions, beginning pus formation, and in not severely infected hemarthroses. Small capsule incision, evacuation of the exudate with a glass drain in most cases for the application of the phenol-camphor treatment to the joint, is to be employed in empyemata of the joint and in severely infected hemarthroses. Wide opening of the joint, when possible in a dependent position, is to be employed in the capsule phlegmons, rich in exudate and destructive. Wider opening without damage to the joint ends, and sacrifice of important tendons and ligaments, is to be used in capsule phlegmons and total suppurations, poor in exudate. Primary typical or atypical resections are rarely done; secondary reactions more often in cases in which the infection cannot be overcome or in fractures with splintering and much damage to the joint ends.

Primary amputation or exarticulation is indicated in crushing injuries with putrid infection, gangrene of the limb, etc. Secondary amputation is done upon the recognition of the failure of the previously named methods and when life is threatened.

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**Treatment of Open Pneumothorax by Immediate Suture of the Thoracic Wall.**—WIEWORSKI (*Zentralbl. f. Chir.*, xliii, 1005) fully agrees with Hanusa that immediate suture of the chest wound is indicated. He would not even wait until the wounded man can be brought to a field hospital, but would have him transferred to the nearest place where he could have the services of a surgeon. The technic is simple: The region surrounding the wound is thoroughly painted with iodine. The gross soiling of the wound is cleansed and the irregular shreds of tissues are cut away with scissors and splinters removed. The wound edges are then approximated by deep silk sutures, taking in the pleura. Narcosis is not necessary. Lung wounds are disregarded. Three sutures in a thoracic wound 12 cm. long will give an air-tight closure. The results in all of the cases were surprisingly good. As soon as the last suture is tied and the sound of the escaping air stops, the groans of the patient cease. The pulse becomes quiet and stronger, the dyspnea ends and the general condition improves. With large lacerations of the lungs and open pneumothorax, the lung sutures and the suturing of the lung into a window opening in the chest wall, belongs to the work of the field hospital.

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**Observations on the Relation of Acidosis to Anesthesia.**—CALDWELL and CLEVELAND (*Surg., Gynec. and Obst.*, 1917, xxv, 22) made observations on the blood of about 120 patients, in the Presbyterian Hospital of New York, together with their acetone and diacetic acid excretion during the period of preparation, operation, and recovery. In the average case undergoing operation, not showing glycosuria, very marked ketonuria nor acidemia before operation, the degree of acidosis induced is negligible, and the choice of anesthetics, so far as the question of acidosis is concerned, is irrelevant. None of the symptoms observed in the routine postoperative course is due to the slight diminution in alkalinity of the blood and tissues, induced by the preparation, anesthesia and operation. With the exception of 1 diabetic patient with obvious severe acidosis, not 1 case in 120 showed an acidosis either from a clinical or laboratory stand-point, approaching dangerous proportions. Acetone and diacetic acid occur in the urine of a certain percentage of patients undergoing operations, and in greatly increased percentage and amounts after operations. The presence of acetone and diacetic acid apparently has no relation to the gravity of the operation or the seriousness of the pathological condition, to the length of anesthesia, nor the postoperative nausea and vomiting. No relation can be determined between the alveolar carbon dioxide tension and the acetone and diacetic elimination, neither in the untreated nor carbonate treated cases, the latter having shown acetone and diacetic acid in the presence of high blood alkalinity. Diacetic acid in the urine is not necessarily a contra-indication to operation. Women show larger percentages and amounts of acetone and diacetic acid, both before and after operation, than men.

## THERAPEUTICS

UNDER THE CHARGE OF

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**The Use of Foreign Protein in the Treatment of Arthritis.**—MILLER and LUSK (*Jour. Am. Med. Assn.*, lxvii, 2010) add to a previous communication in which they reported 24 cases of arthritis treated by intravenous injection of foreign protein. They have continued its use and now report an additional 85 cases. Somewhat smaller doses of the typhoid vaccine (from 40,000,000 to 75,000,000) were given to his patients in this series. They used proteose or pollen protini, in only a few instances, but the results obtained would indicate that, with the proper dosage, improvement similar to that observed after the use of the typhoid vaccine will take place. In the present series there were 45 cases of acute arthritis, 4 of which were gonorrheal, and the period which had elapsed from the onset ranged from two to forty-five days. Previous to coming under the authors' care 33 had been under more or less active drug treatment, usually with salicylates. Of those who had been under previous drug treatment, 29 reported that they had not improved under this treatment, and 4 had been moderately benefited. With typhoid vaccine, 29 of the 45 patients recovered promptly; that is, the pain, redness and swelling disappeared in from one to five days, and usually within from twenty-four to forty-eight hours. From one to four injections were necessary to bring about these results. Of the remaining patients, 8 showed great improvement with only some stiffness or slight pain remaining. Six showed only moderate improvement, and in 2 no benefit was derived from the treatment. Although one of these received eleven and the other thirteen injections. Nine of the patients had recurrence, 5 of those discharged as cured and 4 of those discharged as improved. Seven of these were reinjected and either recovered or showed marked improvement. It is highly probable that the number of recurrences reported is too low due to inability to follow up the cases. In the 4 acute gonorrheal cases in this series, less benefit was derived by the treatment than in those of other origin. Twelve patients with subacute arthritis in all were treated; in 10 the condition cleared up in from three to five days after from one to four injections, although in 2 of them there was still slight stiffness or soreness in one or more joints at the time the treatment was discontinued, clearing up, however, a few days later. Two showed marked improvement after two or three injections, but subsequent injections failed to bring about further improvement. Among those discharged as cured recurrences were recorded in 2; 1 of these recovering after further injection; the other patient did not return to the hospital for further treatment. Nine cases of chronic arthritis with marked acute exacerbation were treated and in 8 the acute symptoms cleared up promptly with from one to three injections. Nineteen patients with arthritis of from

a few months to several years' duration were grouped as chronic arthritis. Only those cases were selected in which there was definite evidence of activity, and ankylosis was not marked. Ten of these patients after from one to five injections showed a definite improvement, the acute tenderness and discomfort on motion was much relieved. The patient became less helpless. As a rule not all the affected joints were benefited. The results, however, were such that it would seem the treatment had been actually beneficial. Not all of these cases have been followed, but there are several in which, after the lapse of several months, the improvement has been maintained. Five showed moderate improvement, and 4 were not benefited. The maximum number of injections given any of these patients was thirteen, being given daily in the beginning and later every two or three days. In 5 patients included in this group the arthritis was apparently of gonorrheal origin, and 3 of these showed such marked improvement that they might be pronounced as cured. This is in contrast to the resistance to the treatment of the acute gonorrheal cases. One of these gonorrheal cases was of seven months' duration and for three months previous to entering the hospital the patient had been compelled to use crutches. After three injections he was able to get out of bed without assistance, and up to the present time (four months) has not had a relapse. It is the very striking results obtained in a few cases of this character which have led the authors to believe that in certain instances the results obtained cannot be equalled by any other of the present methods of treatment. The results in the cases of chronic arthritis are on the whole, however, not especially striking. The tendency to recurrence is great, not unlikely owing to the persistence of a focal infection. It is essential, therefore, that where this method of treatment is employed, it be preceded by the usual efforts first to locate and remove the focal infection. The reaction provoked by the intravenous injection of the typhoid vaccine is severe. There is always a very marked rise in temperature, and with few exceptions a marked chill. The headache as a rule is severe, and nausea of a few hours' duration is not infrequent. In 3 cases, all alcoholics, delirium developed at the height of the fever, in 1 case continuing for thirty hours. Marked dyspnea was observed in a few cases. In only 5 of their patients did Miller and Lusk deem it advisable, on account of the violence of the reaction, to discontinue the treatment after a single injection. No fatalities have occurred as a result of the treatment, but it should be borne in mind that evidence of poor cardiac power or hypertension was considered a contra-indication to the treatment and such patients were not injected. The authors say it is practically certain that the intravenous injection of typhoid vaccine has a decided effect in many cases of arthritis, especially of the acute type. Whether the intravenous use of foreign protein in typhoid and arthritis will be retained as a therapeutic measure depends largely on whether the violence of the reaction with the inconvenience and possible danger to the patient may be considered as outweighing its beneficial results. Perhaps further investigation will show that there are other microorganisms still more active in this respect than the typhoid and perhaps having greater therapeutic value, but also giving rise most likely to even more violent toxic reactions.

## PEDIATRICS

UNDER THE CHARGE OF

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**The Intraperitoneal Injection of Saline Solution.**—BLACKFAN and MAXCY (*Amer. Jour. Dis. Children*, January, 1918, vol. xv, No. 1) state that this method is recommended for the introduction of fluid in the treatment of the severe nutritional disorders of infants especially when, after continued vomiting and diarrhea, marked loss of body fluid results. The ordinary methods often fail because of the presence of vomiting and diarrhea. Intravenous injection is often difficult and it is rarely possible to inject a sufficient quantity without throwing too great a burden on the circulation. The authors have had little success with the subcutaneous method. The patient is placed in the recumbent position with the movements of the arms and the legs restricted by a restraining jacket. The most favorable site for the introduction of the needle is through the linea alba just below the umbilicus. The patient is prepared as for any surgical procedure. The solution is introduced by gravity. Normal salt solution at 100° F. is introduced until the abdomen is slightly distended, which requires from 100 to 250 c.c. The results are noted in a short while. A febrile reaction ranging from 100° to 101° sometimes follows this injection, but it subsides in twenty-four to forty-eight hours.

**Studies of Acid Production.**—SAWYER, STEVENS and BAUMANN (*Am. Jour. Dis. Children*, January, 1918, vol. xv, No. 1) say that major and minor surgical operations, infectious diseases, and diseases of the gastro-intestinal tract are accompanied by an increase of acid production. Children seem more susceptible to acidosis than adults and the authors have undertaken to prove this experimentally on a series of 10 cases. A difference in reaction toward the acid-producing diets was noted by means of the blood and urine analyses. There was also a difference in the time which elapsed before a marked response occurred. The cause of this variation was not determined. The response to the high fat diet was apparently more rapid and greater than to the low calory diet. Starvation does not always produce a marked increase of the acetone bodies in the blood of children. Prominent symptoms of acidosis may appear in less than twenty-four hours on the low calory diet. The most frequent symptoms are nausea, vomiting, drowsiness, irregularity and slowness of the pulse and an increased respiratory rate. The titratable acid of the urine, which is largely due to a preponderance of acid phosphate, increases as a result of the change in the diet before the ammonia. This is accompanied by an absolute increase in the phosphate of the urine without a compensatory decrease of the fecal output. The increased acid elimination is often followed by a period of diminished excretion and this is asso-



ciated with a similar decrease of the phosphate excretion. The increase of the ammonia excretion appears on the second day after taking the acid-producing diet and lasts for several days after the resumption of the normal diet. Creatinin is practically constant and may be used as a standard to determine the accuracy of the urine collection. Creatin is uniformly increased during the period of increased acid production, which is followed by a period of markedly diminished excretion lasting several days. While the nitrogen excretion varies within wide limits, an unmistakable rise during the period of high fat feeding is present. This increase is uniformly accompanied by an increased creatin excretion and may be due to muscle break-down. In this series during the low calory period twice the amount of nitrogen ingested was eliminated through the urine and the increased elimination during the acid period was occasionally followed by retention. In a few cases qualitative test showed the presence of aceto-acetic acid four hours after the taking of the high fat diet. The carbonate values of the plasma of the blood is a reliable index of the severity of the acidosis. The combining power appears to be inversely proportional to the sum of the titratable acid. The average normal plasma carbonate value for twelve children between the ages of four and eight years was 54 volume per cent. In a general way the increase of acetone bodies in the blood is proportional to the severity of the acidosis. The glucose content of the blood is usually decreased during the period of acidosis.

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**The Skin and Throat Manifestations of Heine-Medin's Disease.**—REGAN (*Arch. Ped.*, December, 1917, vol. xxxiv, No. 12) believes that congestion of the throat is an almost constant symptom of poliomyelitis during the early acute stage. It is, as a rule, limited to the faucial mucosa and the pharynx, while the soft palate assumes a deep red color and often a distinct violet-like hue. The surface bloodvessels are not usually congested to any great extent. This violet-like tinge varies in degree and while not by any means typical, it is somewhat distinctive of poliomyelitis when it is marked. A mild degree of inflammation of the tonsils is very common, but follicular exudation is rare, as is also true membrane formation. The uvula often appears unusually small. The buccal mucosa varies only slightly in color. The tongue is usually heavily covered with a grayish or yellowish-white coating with the tip devoid of covering. Gingivitis is present in a small proportion of cases. Rashes are frequent especially in younger children. They appear as early as the second day or as late as the fifth week. Their average duration is about four days. In distribution they show a decided tendency to localize on the trunk, especially on the neck and chest and to a lesser degree on the back, abdomen and face. Bulbar cases rarely show an eruption, but meningitic cases are frequently associated with rashes. The most common variety of rash is the pinpoint to pin-head papular form. It is often preceded by a scarlatini-form eruption, which is usually easily differentiated from the rash of scarlet fever. True maculopapular type of rash is rare. When it does occur it is not easily confused with measles. Herpes labialis are rare. Desquamation is rather frequent.

## OBSTETRICS

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UNDER THE CHARGE OF

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**Pregnancy following Extensive Operation upon the Tube and Ovary, with Removal of the Appendix.**—VINEBERG (*American Journal of Obstetrics*) reports a case of a woman, aged twenty-six years, married twelve months, never pregnant, seen in consultation. She had pain in the left groin and fever for several days. Then the pain shifted to the right lower portion of the abdomen and again to the left side. Upon examination, the abdomen was rigid, the uterus partly retroverted, posterior vaginal vault rigid but no mass could be made out. Ten days later the patient was again seen and was no better. The pain in the right side of the abdomen was very severe. The patient was removed to hospital for operation. The uterus was retrodisplaced and adherent, as were both tubes and ovaries. On the left side the tube was inflamed, the ovary cystic and both were removed. On the right side the ovary was in fairly good condition and was left and the tube opened at its fimbriated extremity. The appendix was found high up beneath the liver in a mass the size of a hen's egg, containing adherent ecceum and ileum; the appendix was gangrenous. The patient made an uneventful recovery and subsequently became pregnant.

**Osteomalacia.**—A case of this condition, comparatively rare in this country, is described by BAILEY (*American Journal of Obstetrics*). The patient was an Italian, married at nineteen years, who had in all thirteen children. After the birth of the eleventh, the patient could not get up when she attempted to walk, and during the next four years she became bed-ridden, with more or less constant pain in the legs, thighs and back. Her joints were not stiff, but, on attempting to walk, she had pain in the legs and extreme weakness. About two months before she again became pregnant there was some improvement. Following this pregnancy she was worse, and about two years before coming under observation both the bones of the forearm fractured while the patient was attempting to put her left arm behind her back. She received no surgical treatment, but after three months she was able to use the arm again. The patient was then for some time in the hospital and x-ray examination showed united fracture of the left forearm and partially united fracture of the neck of the left femur. The patient then returned to her home and became much smaller in stature and fractured her left humerus in attempting to raise herself on her elbow. These fragments did not unite. She was again brought to the hospital after being in labor fourteen hours in her thirteenth pregnancy. The abdomen was greatly protuberant and the head unengaged and the patient was given an anesthetic for examination. While being placed upon the table, the right femur fractured with an audible crack. The cervix was found to be fully dilated and the fetal head above the pelvic brim. The pelvis

was beak-shaped and so deformed that the head could not descend. The child was delivered by abdominal Cesarean section and the patient finally developed, in about two weeks, a bed-sore. She was taken from the hospital against advice and subsequently died in her home. The body was obtained for examination and the entire skeleton found to be extensively diseased by osteomalacia. Among the most interesting explanations of this disease is that given by McCrudden (*Arch. Int. Med.*, 1910, lv, 196 to 630) who found by experiment that calcium phosphate is greatly lessened in these cases while magnesium phosphate is increased, the organic sulphur and phosphorus being also increased. Fehling has advanced the theory that the disease is a trophoneurosis due to reflex stimulation from the ovaries. In the case reported, there was a continued drain of calcium from the patient for eleven years, during which she was either pregnant or furnishing milk for her child and exhausting her supply of calcium. There had been several efforts at recovery but these efforts were finally overcome by repeated pregnancy.

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**Pregnancy Complicated by Cancer of the Cervix.**—ZIMMERMANN, (*American Journal of Obstetrics*) among 3000 obstetrical cases in the Low Maternity of the Brooklyn Hospital, found 2 cases of cancer of the cervix complicating pregnancy. He describes the characteristic case of a multipara, aged thirty-seven years, admitted to the hospital because of intermittent vaginal hemorrhage. Menstruation had been missed for about two months, and three days before admission she had cramps in the lower abdomen and greatly increased hemorrhage. A diagnosis of threatened abortion was made. Upon examination, there was a cauliflower growth from the posterior lip. The os was patulous and the body of the uterus not very mobile, soft and about the size of a four months' pregnancy. As hemorrhage was profuse, the vagina was tightly packed with gauze. On the following morning the ovum was expelled with the packing, followed by gradual involution, but the uterus remained tender on pressure and not freely mobile and there was a small mass in the left broad ligament. The entire uterus was removed and the patient's recovery was apparently good. Within eight months she had a return and died of malignant disease involving the remaining structures of the pelvis within a year. A further case is described of a multipara in labor a little before the eighth month. When admitted to the hospital there was a hard ring about the cervix nearly one and one-half inches thick. Although uterine contractions were vigorous, the cervix did not dilate, and malignant disease was evidently present. Accordingly, the child was delivered by Cesarean section and the entire uterus then removed. The patient made a good recovery.

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**Bichloride of Mercury Poisoning from the Insertion of a Tablet within the Vagina.**—MILLAR (*British Medical Journal*) reports the case of a woman who had been in the habit of taking vaginal douches of bichloride of mercury, who inserted a tablet containing  $8\frac{3}{4}$  grains into the vagina at bed time. The patient seemed to think that this was practically the same as taking a douch. At ten o'clock the following morning she came to a physician's office complaining of pain and swelling of the vulva and told what she had done. Copious

warm douches of water were at once given and a few hours afterward severe pain began in the abdomen, with diarrhea and severe vomiting. Upon examination, the vaginal mucous membrane was practically intact but the external parts were congested and edematous. The patient grew steadily worse and died of exhaustion on the sixth day. An autopsy was obtained which showed the characteristic lesions of bichloride poisoning.

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**Twin Pregnancy in a Horn of a Bicornute Uterus.**—SCOTT and FORMAN (*American Journal of Obstetrics*) describe the case of a multipara who became a third time pregnant when her second child was six months old. During the first four months of this pregnancy she suffered from sharp abdominal pain at irregular intervals. On one occasion the pain was so severe that an abortion was feared but did not occur. When the tenth month of pregnancy came, labor pains began and continued over a period of two weeks and subsided without the expulsion of any material from the uterus. The abdomen remained large and it was suspected that the patient had an ovarian cyst. Ten months after this a third child was born and the delivery was not unusual except for rather severe hemorrhage. Three years elapsed and then a fourth child was born, after a normal pregnancy and a normal labor. Three abortions followed the birth of this child, and nine years after the birth of the fourth child the patient again became pregnant and passed through a normal confinement. In the interval of pregnancies menstruation was regular. The abdomen of the patient remained large and she suffered occasional attacks of pain in the lower abdomen very similar to the pains of labor. These attacks gradually increased in frequency and severity, and twenty years after the uncompleted labor the patient entered the hospital for treatment. On opening the abdomen there was a large sac attached to the posterior wall of the pelvis and to the uterus. This was removed, together with the right tube and ovary which were attached to it. The patient made an uninterrupted recovery. Upon examining the sac, the bones comprising two fetal skeletons were found. On microscopic examination the smooth muscle cells were found in the wall of the sac with other tissues, indicating that the gestation sac was a portion of the uterus. Evidently this sac was one horn of a bicornute uterus and in that portion of the womb there had occurred a twin pregnancy and the skeletons of the fetuses had been retained for twenty years. During this time the patient had been pregnant several times and had been delivered of three living children.

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**The Operative Treatment for Stenosis of the Pylorus in Infants.**—MONNIER (*Revue médicale de la Suisse romande*) has operated upon 4 infants, three, four and eight weeks old, for stenosis of the pylorus. In 1 case the child was so weakened by constant vomiting that the operation seemed a great risk. The child, however, grew immediately better and the vomiting stopped as soon as the operation was completed. None of these infants would probably have survived a more complicated operation. The method employed was that of Rammstedt, which consists in slitting lengthwise the muscular fibers of the pylorus, which are always hypertrophied in these cases. The incision leaves the mucous membrane undisturbed. There

is a separation of 2 or 3 mm. between the cut edges, which makes a gap, in the depths of which the mucous membrane can be seen protruding slightly. No sutures are applied, and occasionally a small omental flap is drawn over to the site of operation, which requires but a few moments. But a few drops of chloroform or ether, or both, are given, and the pyloric region is drawn out through a small opening above the umbilicus. The pylorus was a hard tumor resembling an almond, without any suggestion of inflammatory changes, and with an anemic surface. The incision is carried freely through the serous and muscular coats down to the mucous membrane and the cut edges separated widely, but there is scarcely any bleeding. After the operation the child must be fed very carefully, small quantities only of food being given at frequent intervals. As the child is ravenously hungry the temptation is to give too much. When feeding is limited or when a wet-nurse can be obtained the results are usually very satisfactory.

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**The Umbilical Cord as a Factor in Infant Mortality.**—YOUNG (*American Journal of Obstetrics*) calls attention to the part played by the umbilical cord in producing the death of the infant during gestation and at birth. During gestation, knotting of the cord may cause the death of the fetus at any time. At the time of birth the cord is frequently around the neck, and the importance of this condition depends upon its length and elasticity, the number of coils, and the placental implantation. This coiling of the cord is furthered by unusual activity in the fetus. The condition may be inferred during labor if the head is imperfectly flexed and withdrawn between the pains. If there is shock during pains or symptoms of hemorrhage through placental separation the diagnosis is suggested. The largest number of coils reported about the neck of the child is eight, and if the life of the child is to be saved, immediate delivery by Cesarean section must be considered. A case is described of a primipara, with normal pelvis, who had premature rupture of the membranes and slow labor. Pituitrin was given twice. The head engaged, but between the pains receded very noticeably and shock developed during pains. The patient was delivered with difficulty by forceps and seemed much shocked during the operation. The child was dead, the cord was three times about the neck and pulled to an exsanguinated rope, a noose being formed by the cord. The placenta was attached at the fundus on the posterior wall of the uterus. The cord measured 106.5 cm. Had Cesarean section been employed promptly the child's life might have been saved. In discussion, Barclay drew attention to the fact that a short umbilical cord is rare. The records of the last year at the Maternity of the Manhattan Hospital show but 5 short cords, of which the shortest was 37 cm. in length. Of these only 3 made complications during labor. In 3 instances the condition was recognized before delivery, in which case the child was delivered and the cord torn off 0.5 cm. from the imbilical ring. There was profuse hemorrhage, which was stopped by circular purse-string sutures. In another case the head was on the vulva and receded to an abnormal extent in the interval between pains, and from this the diagnosis was made. In still another there were 2 coils of the cord around the neck. The cord was cut and the child delivered. The cord measured 45 cm. in length. In this case the cord was both short and wrapped about the child's neck, and during delivery the placenta was detached, followed by sharp hemorrhage.

## GYNECOLOGY

UNDER THE CHARGE OF

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**Results of Radium Treatment in Cancer.**—As a result of the use of about 235 mg. of radium in the treatment of 642 cases of cancer and allied conditions at the Collis P. Huntington Memorial Hospital from September, 1913, to January, 1916, DUANE and GREENOUGH (*Boston Med. and Surg. Jour.*, 1917, clxxvii, 359) believe that the following conclusions are justified: (1) Many cases of advanced, inoperable, or recurrent cancer may be given benefit by treatment with radium. (2) In such cases the relief may include one or more of the following advantages—relief of pain, diminution of discharge, rendering discharges less offensive, relief of hemorrhage, diminution in the size of the tumor masses, even to their total disappearance, and the improvement in the general condition of the patient. To these must be added the undoubtedly beneficial psychic effect upon the patient. (3) In a very small number of advanced and apparently inoperable cases, improvement may occur such as to permit a radical operation to be performed. (4) In a certain proportion of cases of superficial non-metastasizing types of cancer (about 35 per cent.) and in a much smaller number of cases of metastasizing cancer, radium is capable of destroying the clinical manifestations of the disease. Sufficient time has not elapsed to report these cases as cured, and they are being kept under observation. In a limited number of cases, recurrence, after apparent destruction of the lesion, has taken place. (5) In keratoses, papillomata, and other benign skin diseases regarded as “pre-cancerous,” radium is effective in destroying the clinical manifestations of the disease in from 48 to 60 per cent. of cases. In the treatment of many tumors and diseases radium has been used with benefit, depending largely upon the extent of the disease, its depth in the tissues and the practical ability to apply sufficient radiation to modify or destroy tissue or tumor growth. The use of radium in prophylaxis of recurrence after radical operation for the cure of cancer is not advised by these investigators. When serious doubt exists as to the complete removal of the primary tumor and when the location of the suspicious area is superficial and accessible and of small extent, radium may be used with benefit; but when a large area is to be considered, as after an operation for cancer of the breast, the difficulties of covering the whole area with sufficient radiation are such that the treatment is not to be recommended. Of the 642 cases of cancer of all types in this series that were treated with radium, 351, or 55 per cent., received definite benefit. Although many cases of advanced carcinoma show no appreciable benefit from radium treatment, on the other hand, in no case in this series did radium appear to have accelerated the growth of the tumor tissue. Of the detailed report of individual types of cases treated that accompanies this article, we shall concern ourselves merely with that part of it that embraces the female generative organs: *Vagina*: 4 cases of cancer of the vagina

received radium treatment. They are all dead, the average duration of life being six months, from the onset of treatment. *Vulva*: 2 cases and also 1 case of cancer of the clitoris, none of which showed any benefit from the treatment. *Uterus*: these cases have been classified as follows: Group 1. Cases considered inoperable and treated with radium which improved enough to justify later radical operation; 5 cases, 3 living, 2 of which are without recurrence at twelve and eighteen months after operation and 1 case free from recurrence for two years after operation, when a local recurrence appeared and the case is now under treatment. Group 2. Cases given prophylactic treatment following a radical hysterectomy; 5 cases, 2 free from recurrence at twelve and fifteen months after operation, 2 recurrent cases and 1 case untraced but free from recurrence eight months after operation. Group 3. Recurrence after hysterectomy; 37 cases, 1 apparently free from the disease, 2 doubtful, 5 living with recurrences while the remaining 29 are dead. Group 4. Recurrence after the use of the curette and cauter; 21 cases, 4 living with recurrence and under treatment, 1 living and without evidence of disease nineteen months after beginning treatment, but since then untraced. Group 5. Inoperable cases; 22 cases, none free from disease, average duration of life after beginning radium treatment was twenty-two months. Of the total 90 cases of carcinoma of the uterus, 7 cases are living and apparently free from disease at periods varying from six to nineteen months after operation, 2 of these cases being treated on a prophylactic basis while the other 5 were recurrent or inoperable cases. *Ovary*: 5 cases of carcinoma of the ovary received radium treatment. Of these, 1 case showed temporary improvement but died fifteen months after beginning treatment. The other cases showed no marked improvement under radium. In connection with the foregoing article it is interesting to note that Boggs (*Am. Jour. Roentgen.*, 1917, iv, 207) states that experience of the past few years has shown that we cannot treat successfully with radium at a greater distance than 2 or a maximum 3 cm. It has been universally accepted that cancerous growths can be promptly and also apparently permanently cured at this depth from the radium tube. However, if the disease is advanced and there is infiltration of the growth into adjacent lymphatics the cure is only apparent. The local growth may disappear, but if metastasis takes place before treatment is given it will progress without regard to the quantity of radium applied or to the length of time it is applied.

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## PATHOLOGY AND BACTERIOLOGY

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UNDER THE CHARGE OF

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**Reaction of the Spleen in Acute Infections.**—The reactions in the spleen under various conditions of disease have always been difficult of interpretation. Much of this difficulty lies in the lack of a clear

conception of the function of the spleen as an organ, as well as in the lack of knowledge concerning the activities of the individual portion of its tissues. This ignorance permits of wide speculation on the part of many observers, a feature which has been taken advantage of by not a few advancing hypotheses difficult of proving or disproving. As is pointed out by EVANS (*Johns Hopkins Hospital Bulletin*, xxvii, 356) there is no thorough agreement upon the nature of the various cell elements present in the normal spleen. To what extent the spleen pulp is active as a hemopoietic organ, what is the nature of the large endothelial cell of the sinuses and what is the relationship between the endothelial cell of the Malpighian body, of the vascular spaces, and of histogenous origin, are questions which require further study. Evans has made a study of the splenic tissues under conditions of various infections. He points out that the reactions may be broadly grouped into two classes of splenic enlargement: (1) with red pulp substance; (2) with gray pulp substance. It is interesting that these groups are fairly sharply defined by the nature of the infection. The red type of the reaction is an acute splenitis found particularly in typhoid fever and its allied diseases; the gray variety is associated with infections by the pneumococcus, staphylococcus and the various streptococci. These splenic reactions are to be recognized in the gross, the red variety being the large spleen with tense capsule and soft, almost diffuent pulp. In it the Malpighian bodies are obliterated. The gray variety shows moderate enlargement with a pulp substance which, though soft, is never diffuent. The pinkish-gray color is uniformly diffused through the tissue and the Malpighian bodies are not to be seen. The types are also distinct on histological examination. The reaction in the red variety consists mainly of engorgement of the splenic sinuses accompanied by a hyperplasia of the endothelial cells of the pulp. In the gray variety more or less congestion may be present but the tissue reaction is distinctly different from the above. In place of the endothelial proliferation of the pulp there is an accumulation of polymorphonuclear leukocytes and other oxydase-containing cells as well as a fair number of lymphocytes. To observe the more or less specific splenic response to particular infections, Evans studied the spleen of rabbits inoculated with a variety of *B. typhi murium* and the pneumococcus. Although the reactions were not so prominent and individual as they are in man, a similarity in the reaction was nevertheless observed. The author points out that although the two types of splenic tumor appear quite distinctive, it is not to be inferred that single varieties of cell elements alone respond in either.

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**The Oxidizing Ferment of the Myelocyte Series of Cells and its Demonstration by an Alphanaphthol-pyronin Method.**—Classifications of the white cells of the blood we have in plenty. The difficulty which confronts the microscopists is the certain recognition of the cells belonging to individual groups. It is true that under normal conditions or common pathological states this difficulty is not so great, but in certain blood diseases the classification of the cells appearing in the blood stream is no easy matter. By the ordinary methods of staining there is little opportunity to indicate the exact nature of the cells spoken of as



myeloblasts and their differentiation from lymphogenous cells is not certain. It has been shown by Winckler, Brandenburg and others that lymphocytes and their accstral cells are devoid of oxidizing ferments while the cells of myelogenous origin commonly contain it. However, even at the present time it is not clear whether the cells in all stages in the development of leukocytes are oxydase-containing. Nevertheless a positive reaction for oxydase within white cells of the blood is accepted as sufficient evidence for excluding them from the lymphogenous series. Various reagents have been used for this demonstration of this intracellular ferment. The guaiac test has been replaced by a more precise method whereby indophenol resulted from the interaction of oxydase upon alphanaphthol and dimethylparaphenylenediamine. This latter method has been in common use and has given, as demonstrated in the work of Evans, a new understanding to many cells in the circulation and in the hemopoietic organs under pathological conditions. One difficulty in making use of the diamine test has been in the transient nature of the reaction. The coloration of the oxydase granules is best observed within a few minutes after the application of the test solutions, from which time a rapid fading takes place. Furthermore, the diamine compound is very expensive and when made up in solution for use, lasts only a few days. GRAHAM (*Jour. Med. Res.*, xxxv, 231) has brought forward an excellent and inexpensive substitute for the demonstration of oxydase granules. He has tested his method upon blood smears as well as upon formalin-fixed tissues. The results have been very satisfactory. By this method the cells are treated with an old solution of alphanaphthol (or by a solution ripened with hydrogen peroxide) and after washing are then stained with an aniline-pyronin solution. The oxydase granules are sharply differentiated by the pyronin staining and are quite permanent. This new method should find a wide application and permit of a better classification of the indefinite white cells of the blood.

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**The Etiology of Scarlet Fever.**—MALLORY and MEDLAR (*Jour. Med. Res.*, xxxv, 209) have found a microorganism in association with pathological changes of the respiratory tract in scarlet fever, which they believe is of etiological significance. The microorganism is a Gram-positive bacillus belonging to the indefinite diphtheroid group. The exact biological characteristics of the organism for comparison with other members of this group have, as yet, not been determined. The bacillus was isolated from the faucial tissues in 5 cases of scarlet fever. No conclusive results were obtained by means of the complement-fixation test nor by animal experiment by the use of this microorganism. The authors place much importance upon the presence of morphologically similar organisms present upon the epithelial surfaces of the pharynx and respiratory tract in cases dead of scarlet fever. They do not, however, make any positive claim for this organism as the cause of scarlet fever.

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**Primary Carcinoma of the Ureter.**—SCHMITT (*Jour. Cancer Research*, i, 461) has collected all the undoubted cases of primary carcinoma of the ureter, beginning with the first reported by Wising and Blix in 1878. Spies, in 1915, published a very complete review including

benign and malignant tumors of both kidney and ureter. The author however, is able to add 3 other cases, besides the 1 he reports in detail, making a total of 20 cases now recorded in the literature. The condition is one seen after early adult life. The sexes appear to be equally affected. The diagnosis is rarely made clinically, since the symptoms come on very gradually. The presence of a painless abdominal tumor the author states, has most often led to a diagnosis of hydronephrosis due to ureteral obstruction. Pain, which may be severe, is a late manifestation, and in its absence a tentative diagnosis of neoplasm has sometimes been made. The author's case might be called a typical one, as it corresponds in general with the others, whose histories are briefly given. The patient was a female, aged fifty-eight years. The chief complaint was diffuse pain in the abdomen, especially low, in the left iliac region. There was a history of persistent constipation suggesting intestinal obstruction. A little over two months after admission and three and a half months after the onset of her illness, the patient died. Autopsy revealed many dense abdominal adhesions between the viscera and the abdominal wall. In the upper left abdomen there was a large retroperitoneal mass to which the jejunum was adherent in a sharply kinked position. The mass appeared to have some relation to the kidney. Other autopsy findings aside from metastases were of interest but rather unimportant. The neoplastic mass was firmly adherent to the abdominal wall, and to the vertebral column from the eleventh dorsal to the third lumbar vertebra. It was cystic, containing cloudy fluid and necrotic debris. The body of the third lumbar vertebra had almost been destroyed by the newgrowth, which also infiltrated the psoas muscle. The cavity of the tumor measured 10 x 10 x 15 cm., and its wall averaged 2 or 3 cm. in thickness. The wall consisted of a friable pink tissue on a firm white base. The upper boundary of the mass was higher than the upper end of the ureter. The occlusion of the ureter by the growth had led to a dilatation of the renal pelvis. The lower extremity was continuous with the ureter, which could be followed as a solid cord for a distance of 3 cm. into the mass. Below this point the ureter was normal. Sections showed the tumor to be a primary cancer of the ureter, further described as of the transitional cell variety. Metastases were found in the portal channels of the liver, beneath the capsule of the left kidney, and in the bodies of several vertebræ. The lung and liver, it may be noted, are the usual sites of secondary growth in tumors of this sort. The relation of calculi to carcinoma of the ureter is mentioned in this connection, but a definite suggestion as to the etiology is not made.

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**Experimental Typhoid Cholecystitis with Cholelithiasis.**—The importance of a typhoid infection locating in the gall-bladder is by no means new. It has been brought to our attention through the finding of the typhoid bacillus in the gall-bladder in virtually every case of typhoid fever, and also in the evidence that human carriers of this infection possess an infected nidus in this viscus. Furthermore, there is evidence that not a few of the cases of chronic cholecystitis have their beginning in typhoid fever. The association of gall-stones with these chronic inflammatory processes of the gall-bladder is also well known and has been shown to have a direct relation with a typhoid infection.

EMMERICH and WAGNER (*Centralbl. f. Allgem. Path.*, xxvii, 433) carried out a series of experiments in which the results strongly confirm the observations made in the human. They immunized rabbits, by means of vaccines, against the *B. typhosus*. These animals were then inoculated with living cultures directly into the gall-bladder. Observations were made upon these animals during a period of eighteen months and, by the examination of individual rabbits at various periods, the sequence of pathological changes in the gall-bladder was observed. Various grades of inflammation were observed, the most interesting being those in the later months when chronic processes became evident. Fibrosis of the gall-bladder with destructive or hyperplastic reactions in the mucosa associated with a shrinkage of the wall, were very similar to the lesions seen in human cholecystitis. The curious overgrowth of the glandular elements of the mucosa frequently appearing to invade the deeper submucosa is noteworthy. In a fair number of the animals there was the development of gall-stones consisting mainly of pigment deposit. The stones were multiple and of irregular size and shape. They contained relatively little cholesterin. The majority of animals also became chronic carriers, so the *B. typhosus* could be isolated from the stools or intestinal contents.

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## HYGIENE AND PUBLIC HEALTH

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UNDER THE CHARGE OF

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**Health of Food Handlers.**—HARRIS and DUBLIN (*Monograph Series*, No. 17, Department of Health, New York City) report the result of intensive examination of 1748 food handlers examined at the Occupational Clinic during 1915 and 1916. These intensive examinations were made possible by the coöperation of the American Museum of Safety, and are typical for the entire number of food handlers, 44,042 examined at the Clinic and 33,000 by private physicians during the same period. The results of the examinations were classified, tabulated, and analyzed by Dr. L. I. Dublin, statistician of the Metropolitan Life Insurance Company. The 1748 food handlers represented the following occupations: Waiters, 695 persons; waitresses, 211 persons; cooks, male, 278 persons; cooks, female, 110 persons; other kitchen employees, 180 persons; bakers, 274 persons; total, 1748 persons. The conditions found were as follows: In the entire group there were 10 cases of active tuberculosis, 12 of suspected, and 3 arrested tuberculosis. Among waiters

were found 5 positive and 2 suspected cases; 41 persons gave evidence of active or suspected syphilis, of which 37 occurred among waiters. This group furnished 46 individuals with flat feet and a similar number with varicose veins. Among waitresses, of whom 211 were examined, 65.8 per cent. showed anemia and 62 per cent. had varicose veins; 17.1 per cent. were reported as suffering from some form of menstrual disturbance. Four waitresses were discovered to have syphilis. The predominating defect among cooks was organic heart disease. There were 32 who showed cardiac disease. In addition, also, 1 active, 1 arrested, and 2 suspected cases of tuberculosis and also 1 active and 5 suspected cases of syphilis were found. Of these cooks 161 had very marked disturbance of the digestive functions. Among bakers no tuberculosis or active syphilis was demonstrated, but 38 cases of chronic bronchial conditions, consisting of 9 chronic bronchitis and 29 pulmonary emphysema; 30 had organic heart disease and 33 anemia. The importance of the examination of food handlers is shown both from the stand-point of protection of the health of the community and opportunity of studying in occupational groups, the preventing of disease, and in order to discover incipient pathological conditions that would otherwise make great progress before being discovered. Finally, it is shown that the lack of uniformity in clinic standards and methods of classification makes the reports that have thus far been published by others working in the field of industrial hygiene less valuable than would be if such uniformity were present.

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**Experiences with the Louse Nuisance.**—HASE (*Zentralblatt Bakt.*, Part 1, p. 153) reports the following: One year of warfare has elapsed and much of interest has been learned with reference to body lice. There are persons who acquire immunity to the painful sensation caused by the bite of the parasite. Some persons are not attacked at all, some are hypersensitive, and some acquire immunity to the bite gradually. This explains the fact that the greater part of the population of Russian Poland is indifferent to the louse nuisance. It appears that a subject which is immune to louse bites is not immune to the bites of other parasites such as bed-bugs, fleas, and mosquitoes. Of all commercial preparations sold for the purpose of destroying lice not one has been found to be of real lasting value. Many of these preparations are highly odorous and some are indeed dangerous. The author cites an interesting list of not less than 181 proposed remedies. One called "Insectol" is advertised as being of particular value and calls for the ingestion of pills containing milk-sugar and the extract of the parasite. The assertion often made that those who are constantly handling horses are free from lice has not been verified. Profusely sweating individuals do not seem to be more affected than scantily sweating individuals. Of peculiar interest is also the observation that lice will shun an old dirty shirt and underwear saturated with perspiration while they seem readily attracted by fresh and clean fabric. Apparently the high temperature and humidity of the air between the body and the fabric do not seem to agree well with the parasite. A louse will always look for the cooler parts of the clothing. The soldiers claim that the lice made themselves much more obnoxious while the soldiers were at rest and comparatively cool. It has also been noted that the number of lice is

much more diminished in trenches where ants were plentiful. Soldiers took advantage of this observation by placing their shirts upon the ant hills. The author discusses briefly the factors which are essential to prevent the spread of the louse nuisance among soldiers. It is a very difficult and tedious procedure to free trenches of lice.

**The Present Status of Birth Registration in American Cities and its Relation to the Infant Mortality Rate.**—DUBLIN (*Tr. Seventh Annual Meeting of the American Association for the Study and Prevention of Infant Mortality*) presents the results of an inquiry into the completeness of birth registration in American cities in the years 1910 to 1915. He received reports from 168 cities and to these applied certain tests intended to measure the accuracy and completeness of birth registration. Of the cities reporting many had fewer births than the population under one year of age and a considerable number had a birth-rate much lower than could be expected in any normal American community having anything like complete birth registration. The birth-rates for many of the cities varied markedly from the average for all—a variation than can be explained only on the basis of incomplete birth registration. On the other hand, the birth-rate in a considerable number of the cities increased markedly during the period under consideration, thus showing that the proportion of births registered was increasing from year to year. Few can doubt in the face of the figures presented that birth registration in most American States and cities is woefully inadequate. The writer then shows how the conditions of birth registration in any community affects the infant mortality rate. Since this rate is based on the proportion of infant deaths to 1000 births, incomplete registration of births makes the rate too high. It also makes it impossible to compare the infant mortality rates for different cities in which the proportion of births registered varies. An increase in the proportion of births registered from year to year may also produce an apparent decline in the infant mortality rate even though the actual status of infant mortality remains the same. The writer shows how the supposed recent decrease in infant mortality in some of the cities studied is in reality the result of an increase in the proportion of births registered from year to year. He feels that infant welfare work attention for the next few years should be concentrated on the problem of birth registration. "We should work to establish a registration area for births which will be nation-wide and as accurate as it is extensive."

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DR. GEORGE MORRIS PIERSON, 1913 Spruce St., Philadelphia, Pa., U. S. A.





LIEUTENANT-COLONEL JOHN McCRAE

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JOHN McCRAE, B.A., M.D., M.R.C.P. (LONDON),  
LIEUTENANT-COLONEL, C. A. M. C.

IN FLANDERS FIELDS.

In Flanders fields the poppies blow  
Between the crosses, row on row,  
That mark our place; and in the sky  
The larks, still bravely singing, fly  
Scarce heard amid the guns below.

We are the Dead. Short days ago  
We lived, felt dawn, saw sunset glow,  
Loved and were loved, and now we lie  
In Flanders Fields.

Take up our quarrel with the foe:  
To you from failing hands we throw  
The torch; be yours to hold it high.  
If ye break faith with us who die  
We shall not sleep, though poppies grow  
In Flanders Fields.

(LONDON "PUNCH," 1915.)

JOHN McCRAE, physician, soldier and poet, died in France from pneumonia, complicated by meningitis, on January 28, 1918. He was born in Guelph, Ontario, in 1872, the son of Colonel and Mrs. David McCrae, who survive him. His primary education was received in the Guelph schools, and later he entered the University of Toronto, graduating in arts in 1894 and in medicine in 1898, being the gold medallist of his year. He was an intern in the Toronto General Hospital, the Garrett Hospital at Mt. Airy, Md., and the Johns Hopkins Hospital, and then accepted a Fellowship in Pathology at McGill University under Professor J. G. Adami, to whom he became most intimately attached. In 1904 he received the conjoint degrees of M.R.C.S. and L.R.C.P., and later took the M.R.C.P. (London). He had lived in Montreal since 1900, and his work in medicine was chiefly identified with the Medical School of McGill University and the Royal Victoria Hospital. For several years he served as pathologist at the Montreal General Hospital, primarily under the guidance of Wyatt Johnston, and after his



death was in charge of the department. For a number of years he was professor of pathology at the University of Vermont. In 1905 he was elected associate physician to the Royal Victoria Hospital and physician to the Alexandria Hospital (for infectious diseases) in Montreal. He continued his association with the department of pathology, and until his death held the dual position of lecturer in pathology and lecturer in medicine at the Medical School, McGill University.

John McCrae was a born teacher. He loved the simple exposition of the pathology of disease and avoided at all times beclouding the subject with the abstruse and intricate. His demonstrations were impressive and sharp was his criticism, each point being made with a snap which reminded one that he was a student of Carlyle. If contrast was required in teaching it was used even to the grotesque. To the student it was a new departure from the uninspiring lecture, and he revelled in it. I have repeatedly met students who had sat under him and they never stinted their praise of his teaching. His simple methods demanded a firm rule and his class-room reflected a stern but congenial relation of master and student. The ward teaching was his particular delight, and when didactic lectures fell to his lot he converted them as nearly as possible into practical demonstrations by bringing as much pathological material to the lecture room as was possible. The students loved him for the interest he always displayed in their difficulties and because he showed the human side in medicine. They learned from him the unselfish duty of the physician to human distress in all walks of life. They loved him, too, because he never feared to step from the dignity of the teacher to the level of the student.

In 1899-1900 he served with the artillery in South Africa, saw much active service and was in many engagements. Although serving as an artillery officer, he often acted as a medical officer when need required. His military activities brought him the Queen's Medal, with three clasps, and later he was appointed commanding officer of his battery. McCrae had much of the soldier in his make-up. His carriage, his approach and his appearance before an audience marked him of soldierly character. His method of dealing with others was always with that straightforward, square front which we are pleased to recognize as the attribute of a true soldier. He lent no patience to trivial quarrels, and often he would appear as the peacemaker, particularly amid the factions of a junior

faculty who everywhere are Quixotic in their grievances. On the other hand, he would have nothing with the peace-at-any-price party when a quarrel founded upon rights and principles was at stake. He was a man of few words but of decided action. Of his South African experiences he rarely spoke, but we have a number of poems, which though telling us little of the actual warfare, spoke volumes of the thoughts of the man. In 1910 he was invited to accompany Earl Grey, then Governor-General of Canada, on his trip through western Canada, across Hudson Bay and return by way of Labrador. The members of this party never failed to refer to the interest and pleasure which John McCrae infused into the trip. Earl Grey said that "they had travelled 3000 miles and McCrae had a story for each mile."

At the outbreak of war in 1914 McCrae had just arrived in London. He sailed to Canada offering his services and was appointed surgeon to the First Brigade of Canadian Artillery. He was with the guns along the Ypres sector for a continuous period of fourteen months, and was in the thick of the engagements where the Canadian forces made an undying name for their valor. His brigade was behind the area where the first gas attack was delivered and his description of their moving up to hold the front line was most graphic. They were under intense fire for seventeen days, and on one occasion a shell came through his dressing station, but he escaped injury. When in the service of his country he was a man of few words, and few there are who have an appreciation of what he endured. His health was undermined by the strain of constant duty and the conditions under which the men were living in the early period of the war. He did not realize this: in fact, he was reproving himself for the lack of greater sacrifices which he deemed it his duty to make. It was only through the strong appeal of his friends that he consented to accept the post of internist at a base hospital (McGill Unit).

In his medical duties he was equally severe with himself. He sacrificed his all for the comfort and welfare of the men under his charge; he was keenly desirous that all the invalided should have the last ounce of care provided, to restore them to health as early as possible. He served for over two years as chief in medicine in the McGill Unit. Just before his death he had been appointed consultant to one of the British Army areas, the first officer of the overseas forces to be so honored. News of this came on the day on

which he was stricken with pneumonia. The attack at first seemed mild, but meningitis developed on the third day and death came two days later.

In medicine John McCrea will be known to us for his admirable teaching, and a number of researches of which his investigations on the relation of extensive superficial burns to duodenal ulcers, acute mycotic aneurysm of the aorta, necroses of the liver and a clinical study of scarlet fever are among the most important. He was co-editor with Professor Adami in the writing of a *Text-book of Pathology*. He edited the department of Pathology and Bacteriology in this JOURNAL for a number of years. However, he is much more widely known to a general audience for his literary essays and poems. During the present war the poems given herewith are among his best. "In Flanders Fields" has received favorable criticism everywhere, and has been republished the world over.

John McCrae leaves a host of friends to mourn his untimely end. All will sorely miss him and his genial presence. Those who knew him will carry forward his torch, not forgetful of the living spirit of the man and a character as true as steel. His last poem, "The Anxious Dead," may almost be regarded as an answer to "In Flanders Fields."

#### THE ANXIOUS DEAD.

O guns, fall silent till the dead men hear  
 Above their heads the legions pressing on  
 (These fought their fight in time of bitter fear  
 And died not knowing how the day had gone).

O, flashing muzzles, pause, and let them see  
 The coming dawn that streaks the day afar:  
 Then let your mighty chorus witness be  
 To them, and Caesar, that we still make war.

Tell them, O guns, that we have heard their call,  
 That we have sworn, and will not turn aside,  
 That we will onward, till we win or fall,  
 That we will keep the faith for which they died.

Bid them be patient, and some day, anon,  
 They shall feel earth enwrapt in silence deep,  
 Shall greet, in wonderment, the quiet dawn,  
 And in content may turn them to their sleep.

(LONDON "SPECTATOR," 1917.)

OSKAR KLOTZ.

THE  
AMERICAN JOURNAL  
OF THE MEDICAL SCIENCES

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ORIGINAL ARTICLES

SPINA BIFIDA OCCULTA:\*

- (1) WITH EXTERNAL SIGNS, WITH SYMPTOMS.
- (2) WITH EXTERNAL SIGNS, WITHOUT SYMPTOMS.
- (3) WITHOUT EXTERNAL SIGNS, WITH SYMPTOMS.
- (4) WITHOUT EXTERNAL SIGNS, WITHOUT SYMPTOMS.

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By spina bifida one ordinarily means, and the dictionaries so define it, a cleft or deficiency in the bony column with a lesion of the spinal cord or its membranes—usually a protrusion (meningocele, myeloele, or meningo-myeloele). This is, I think, a wrong use of the words. Spina bifida means bifid spine, and that individual has a spina bifida who has a cleft in the spine, whether or not there is protrusion of the spinal cord structures. In 1875, when Virchow<sup>1</sup> reported what was supposed to be the first case observed, he coined the term “spina bifida occulta” to indicate a type of spina bifida in which the lesion was concealed beneath the skin. In a search of the literature as far back as 1825 I found, however, two earlier cases<sup>2</sup> that belonged to this type of spina bifida,† and up to 1910 I found recorded about 85 cases. In these the lesion was indicated

\* Read, by invitation, before the New Hampshire Medical Society, May 16, 1917.

† The satyrs of the ancients may well have been suggested by instances of spina bifida occulta with short sacral “tails” and club-feet. Concerning satyrs, see Pauly, *Realencyklopädie der Klassischen Alterthumswissenschaft*.

externally most often by a distinct hypertrichosis over the cleft, somewhat less often by a congenital lipoma symmetrically situated over the cleft, occasionally by a nevus, telangiectasis, or scar, or sometimes by a combination of these. Such a spina bifida occulta is most often found in the lumbar or lumbosacral region, but it may occur in the dorsal or even the cervical region. It usually involves only a few vertebral arches, but it may extend through the *greater part of the spinal column*. The "woman with the horse's mane,"<sup>3</sup> exhibited many years ago in the "dime museums," with a luxuriant mane of hair over the midline of her back, was an instance of such an extensive bifidity. Mere hairiness of the lumbosacral region, which is noted in many individuals, is not indicative of a spina bifida. Such a well-marked hypertrichosis with long hairs as is shown in Fig. 19, is, however, a pretty safe indication that a spina bifida occulta is present, and probably most of the cases of sacral hair growth studied by anthropologists some years ago as an atavism, or a stigma of degeneracy, are instances of this congenital deformity, as first suggested by Recklinghausen.<sup>4</sup> I have found some very interesting records of such lumbosacral hair growth in several members of a family, however, and spina bifida occulta is not an hereditary phenomenon. The hypertrichosis may not appear, or develop prominence, until puberty.

The congenital lipoma associated with spina bifida occulta is not freely movable, but is somewhat attached to the underlying aponeurosis, and is usually quite circular in outline (Fig. 2). In 4 cases operated upon I have confirmed the interesting observation recorded by A. Jacobi,<sup>5</sup> many years ago, that congenital lipomata differ from the other varieties in being unencapsulated and very finely lobulated, in which respect they are much like subcutaneous fat. Not every case of congenital supraspinal lipoma has a bifidity associated with it.

In several cases of spina bifida occulta scoliosis or other spinal deformity is also present, and sometimes there are other congenital malformations.

In his recent work on the *Surgical Diseases of the Spinal Cord* Elsberg explains the phenomena of spina bifida occulta in the following manner: At birth the cord extends down to the lower end of the spinal column; as the individual grows the cord recedes, relatively speaking, until its lowest end is at about the first or second lumbar arch; if, therefore, any nerve roots are congenitally herniated through a spinal column dehiscence, these will undergo stretching as the disproportion in length between the bony and medullary columns develops with the growth of the individual. Of course, however, this must not be accepted as the entire explanation for the following reasons:

1. In some cases with symptoms there is no hernia of the spinal cord structures.

2. In a few recorded cases, symptoms developed as early as the second year after birth.
3. In some cases, as in one here recorded (Helen H.), the lesion is a teratoma (fibromyolipoma) of the cauda equina.
4. In some cases there is an exostosis in the canal compromising the cord tissues.
5. In many cases there is ample clinical evidence of a lesion in the cord itself.
6. At autopsy in some of the recorded cases dilatation of the spinal canal or degeneration of various tracts has been demonstrated.

At operations and autopsies these abnormalities have been found: A cleft of varying length or breadth in one or more arches accompanied by one of the following conditions: (1) The cleft may give passage to a distinct meningocele; (2) the cleft is closed by a tough membrane adherent to the overlying skin or non-encapsulated fat and connective tissue; (3) the membrane is perforated by a dense band attached to the subcutaneous tissues without and compressing the cord structures within; (4) lipomatous tissue within the canal is concealed by this membrane; (5) the cleft discloses the bulging dura mater; (6) an exostosis within the canal compromises the cord tissues; (7) a myofibrolipoma extends through the cleft into the bony canal distorting and compressing the cord and its nerve roots; (8) dilatation of the medullary canal; (9) degeneration of cord tracts.

The symptoms arising from spina bifida occulta usually appear during adolescence or early adult life, but not rarely they develop during childhood, and occasionally they first appear during middle life. These symptoms may be one or more of the following: Incontinence of bladder or rectum; sensory paralyses; motor paralyses; disturbances of the reflexes; trophic ulcerations and gangrene. Symptomatically, therefore, spina bifida and spina bifida occulta are one. It must be noted, too, that pathologically spina bifida and spina bifida occulta do not greatly differ. Tumor tissue sometimes accompanies evident spina bifida; hypertrichosis sometimes does; an evident meningocele is occasionally partially concealed by a congenital lipoma; and, finally, there are reasons for believing that a spina bifida sometimes shrinks, leaving only scar tissue or other index to a spina bifida occulta.

Of the type of spina bifida occulta with symptoms and with external signs, by which I mean lipoma, hypertrichosis or nevus, the following 3 cases are interesting examples.

GROUP I.—*Spina Bifida Occulta, with External Signs, with Symptoms.*

Sigrid H., female, aged eighteen years, came under my care in December, 1907, for an extensive ulceration of the inner and flexor aspects of the great toe of the left foot, indolent in appearance, and with foul discharge.

She was a native of Jönköping, Sweden, where, at the age of seven, the second left toe was ulcerated from what was presumed to be frost-bite. This ulceration recurred each winter and, at the age of twelve, partial amputation of the toe was required.

Three years later (aged fifteen) the stump of the toe ulcerated and the phalanges necrosed. Six months later the fifth toe ulcerated, refused to heal, and was amputated.

She never had vesical, intestinal, or motor disturbances. She never noticed anesthesia in either foot or leg. No lightning pains, but these ulcerations were mildly painful. At the appearance of each fresh ulceration she said she had malaise, headache, nausea, and fever, and the toe would first appear red.

Observations of this patient and the next one to be reported confirmed this statement: preceding and accompanying each fresh ulceration, both patients felt ill and had a rise of temperature to 103° or 104°. The appearance of a fresh ulceration could thus be accurately predicted.

The girl was referred to my surgical from the neurological department of the Mount Sinai Hospital Dispensary as a purely surgical case, and with the assurance that there was no neurological lesion. I mention this not in criticism, but to illustrate how even a trained neurologist may overlook a spina bifida occulta until a single experience teaches him to be on the lookout for it.

The foul ulceration for which the patient came to me has been briefly described. The first phalanx was necrotic. The wound was laid open and this bone was removed. Slowly the wound healed, *without granulating*, after the head of the first metatarsal spontaneously discharged. Specific medication seemed to exercise no influence. The dorsalis pedis, popliteal and posterior tibial vessels pulsated normally. The urine was negative. The foot condition and the patient's nativity suggested the possibility of leprosy.

Dr. Prince A. Morrow, who was kind enough to examine the patient for me, wrote: "I think the diagnosis lies between syringomyelia and leprosy, probably the latter. I have seen quite a number of unilateral manifestations due to leprosy, although the dystrophic changes are usually symmetrical. The rather characteristic plantar ulcers and the anesthetic ulcers are in favor of leprosy."

In April, 1908, the two remaining toes (third and fourth) ulcerated and the two last phalanges of these were removed, leaving stumps. The foot was then quite edematous but not painful, although there developed at this time a plantar ulcer near the base of the third toe (Fig. 1). Smears from the ulcers showed no *lepra bacilli*.

I had the patient admitted to the second surgical division of the Hospital (Dr. Lilienthal) for further study. I abstract from her history the following positive findings:

Over the lower lumbar and upper sacral region extending down

from the third lumbar vertebra is a circular tumor about four and a half inches in diameter symmetrically situated over the midline

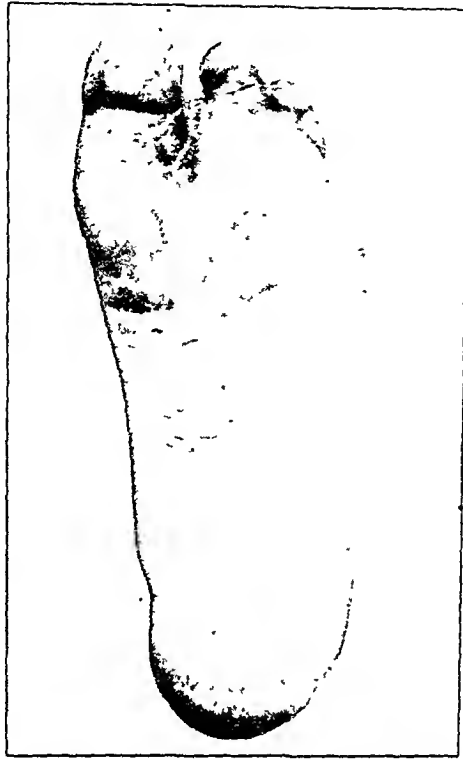


FIG. 1.—Sigrid H., September, 1908. Plantar ulcers at base of third toe and over the head of the second metatarsal. Note stumps of toes.



FIG. 2.—Sigrid H. Congenital lipoma over spina bifida occulta.

(Fig. 2). It is about one and a half inches thick in its center, of doughy consistency, painless and not tender, moderately movable over the deep structures and adherent to the skin at its center. This



tumor was present since birth and has grown with the patient. In the spine no cleft can be felt. No hypertrichosis. The left foot is as above illustrated and described. Blackish, rugous epithelium covers part of the third toe where it abuts against the great toe. The plantar ulcer is small, deep, conical, lined with granulations, but does not extend to the bone. Reflexes: abdominal—right, active; left, absent: gluteal—absent on both sides: knee-jerks—right, feeble; left, absent: achilles—right, feeble; left, absent. No Babinski or

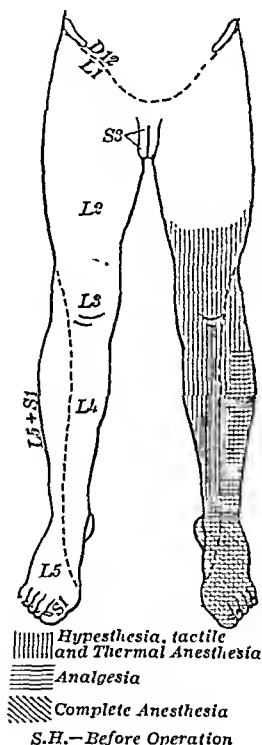


FIG. 3

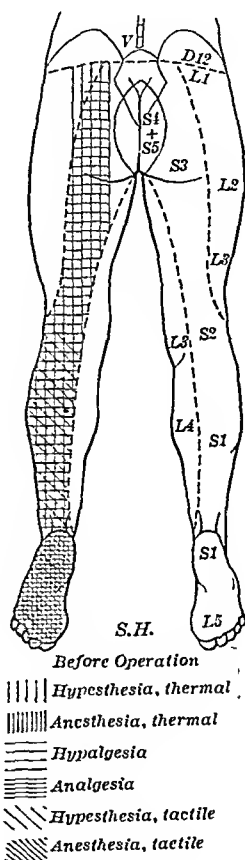


FIG. 4

Oppenheim phenomenon. Motor power of lower extremities normal and equal. Gait normal. No ataxia. Tests show sensory paralyses of the left lower extremity as illustrated in Figs. 3 and 4. Roentgenogram shows a cleft in the *left* lamina of the fourth lumbar arch. The fifth lumbar arch is not of normal shape (Fig. 5). Clinical diagnosis: spina bifida occulta associated with congenital lipoma over the lower end of the spine; cleft in the fourth lumbar arch with a lesion involving the posterior fourth and fifth lumbar and first, second, and third sacral roots or cord segments.

Fig. 6, taken from Sobotta's *Anatomy*, illustrates how pressure on the cauda equina at the level of the fourth lumbar vertebral arch would affect the posterior roots below the level of the third

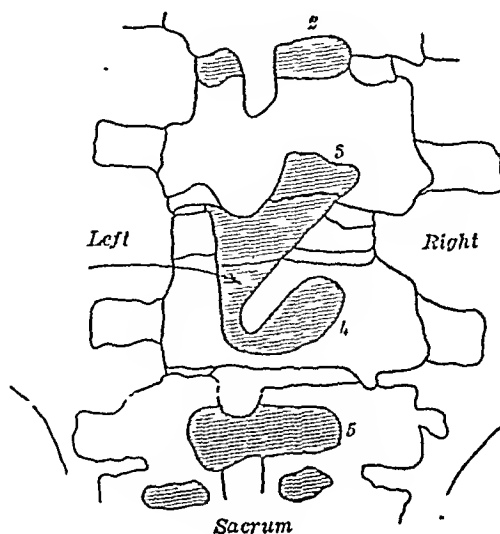


FIG. 5.—Sigrid H. Tracing of roentgenogram of lateral spina bifida.

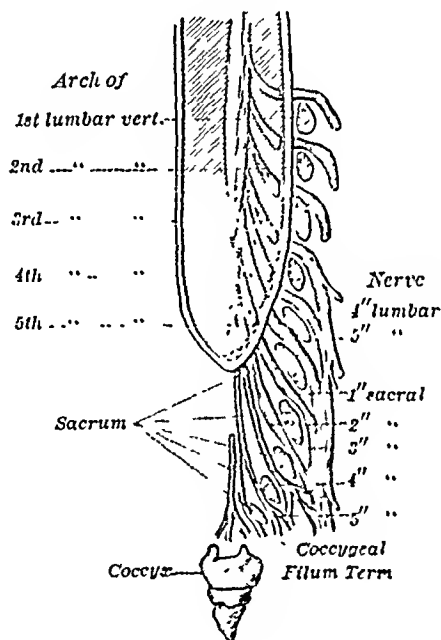


FIG. 6.—Emergence of the posterior nerve roots between the bony arches. Illustrating that pressure on the cauda equina at the level of the L4 arch would affect these roots below the L3 root. (After Sobotta.)

lumbar root, and how, if sufficiently circumscribed, some of the lumbar and sacral roots on one side only might be involved. This was, in fact, just the condition found at

Operation (Brickner and Elsberg), July 3, 1908. Curvilinear incision over the upper border of the tumor, which was found to be a large collection of unencapsulated fat arranged in very small lobules like subcutaneous fat and practically free from bands of fibrous tissue. Incision was carried through this down to the lumbar aponeurosis and the spinous processes. These were found normally disposed, but just to the left of the fourth lumbar spine there was a distinct hiatus in the muscles—an opening lined with fascia which here dipped down toward the spinal canal. This opening easily admitted the finger-tip. Through it issued a strong, apparently dense columnar structure. This structure terminated in the lipoma, but it had no attachment to the skin. With some of the attached fat it was dissected free and dragged through the opening. Incision through the fibrous envelope revealed a serous lining, within which were several nerve fibers. A probe could be passed along these into the spinal canal, and cerebrospinal fluid escaped alongside it. The dural extension thus exposed was further opened, revealing that the hernia was a meningeal sac containing four or five distinct nerve roots of the cauda equina, which bent upon themselves and reëntered the spinal canal. At the point at which these roots were flexed they were found somewhat adherent to the sac, which was at this point much constricted. Distal to this point the meningocele then expanded, but no fluid was noted in this expansion.

The sac was removed, the nerve roots were reduced into the spinal canal, and the dura was sutured over them. The lumbar aponeurosis was closed over the hiatus by a plastic operation.

Following the operation the patient complained of numbness in both lower extremities for a few days, but there was no other untoward effect, and the wound healed *per primam*. Soon after the operation the patient volunteered the statement that her left lower extremity felt more normal, more like the right, than it had for many years before, and improvement was noted in the sensory paralysis, as indicated in Figs. 7 and 8.

Pathological examination of the amputated sac and of the adherent fat revealed no features of special note.

The patient was discharged from the hospital August 4 and readmitted August 25. The ulceration in the third toe had progressed and the plantar ulcer had also increased in size, exposing the head of the second metatarsal bone.

By September 28 these ulcers were healed without any bone necrosis, and the patient was again discharged with a raised sole on her right shoe and crutches.

In November the plantar ulcer reopened, as usual with a rise of temperature to 103°. Surrounding the ulcer there developed a thick, soft callus in spite of the fact that the patient had not put her foot on the ground for many months. During the next few

months the ulcers improved and relapsed and others developed. The patient was readmitted to the hospital.

July 26. Typical Pirogoff amputation (Brickner). All the bloodvessels appeared quite normal. Primary union.

Pathological report of the amputated foot showed—to summarize—practically normal vessels, but marked bone atrophy. This atrophy was found in portions of the bone remote from the inflammatory process. The nerves of the foot showed no degenerative changes. In the immediate vicinity of the ulcers there were moderate inflammatory changes in the nerves.

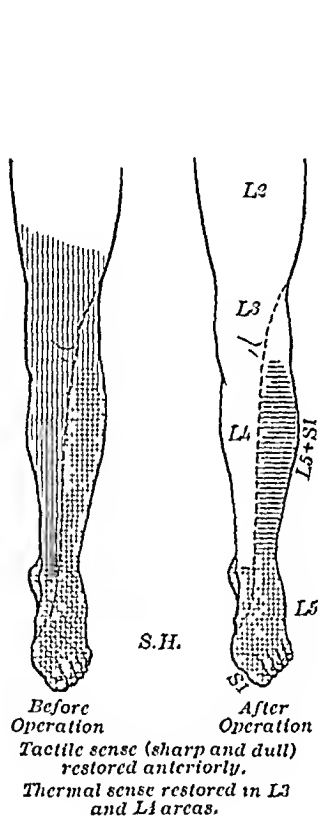


FIG. 7

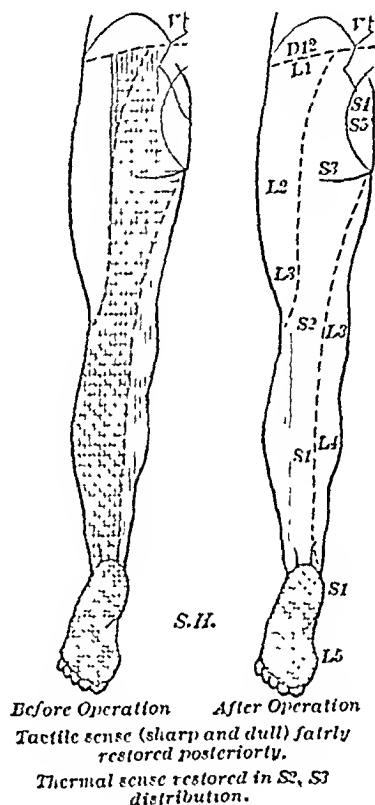


FIG. 8

Contrary to advice the patient insisted upon wearing a shoe containing a cork foot. The pressure of this cork against the anterior aspect of the stump caused an ulceration of the skin within a month after the patient was discharged from the hospital.

Between October, 1909, and May, 1910, the patient neglected treatment, reporting but rarely, the skin necrosis meanwhile extending into a large shallow ulcer surrounded by a dense callus. The raw area was granulating, bled easily, and would probably have healed under good treatment if the patient would have abandoned the shoe, which she insisted upon wearing.

I lost track of her between May, 1910, and January 30, 1911, when she reported again. The ulceration was then much reduced in size, but a gangrene of the heel portion, extending almost to the bone, was present.

February 6, 1911. Osteoplastic amputation through the leg (Brickner). Primary union. Discharged from the hospital.

Soon after that I lost all trace of the patient until in the winter of 1917, through the courtesy of Dr. John Moorhead, I saw her again in the Harlem Hospital. Since my last preceding note she had married and had two healthy children, free from deformity. She had no difficulty in parturition, had no bladder or rectal trouble. During the past year she had lost the fourth and fifth toes of the *right* foot following infection of a corn. She had gone to the Harlem Hospital because of a deep indolent ulceration of the amputation stump (left leg), which had been increasing in size for the preceding six months. During all these six years she had worn an artificial leg pressing against the stump and from time to time had had superficial ulcers, which, however, healed. This deep ulceration did not extend to the bone, and an x-ray picture showed that the bone was not at fault.

Sensory examination in March, 1917, showed in the outer half of the stump below the knee, thermal and tactile hypesthesia as previously, but the right foot and the lower portion of the right leg posteriorly now also show thermal and tactile hypesthesia. The large, deep ulcer of the stump gradually healed.

Whether or not the release of the nerve roots in the spinal hernia obviated any other troubles (*e. g.*, vesical) it would be mere speculation to say.

Our experience with this case suggested to Dr. Elsberg the diagnosis in the case of the following patient, whom he had had under observation for several years at Montefiore and Mount Sinai Hospitals:

Helen H., aged twenty-six years, single, hairdresser. No member of the family, direct or collateral, had had a similar trouble. One sister has a congenital club-foot, unilateral; no other congenital deformities in the family.

Patient entirely well until nineteen. Then, in 1901, she noticed two suppurating ulcers, the size of dimes, in the calf of the left leg, which had appeared spontaneously and painlessly and healed painlessly in two weeks. A month later severe shooting pains in the calf of the left leg and especially the left foot. These continued for a few weeks, when ulcers appeared on the fifth toe and on the sole of the left foot, which swelled. These healed and broke open again repeatedly during the next nine months, and the toe was then amputated. Sensory paralysis was then noted in the other toes, and later in the left foot, leg, and thigh. During the next few years she similarly lost the second, third, and fourth toes, and had ulcers

of the sole and heel of the same foot. She had no urinary disturbances, but had had diarrhea for several weeks before admission to the hospital, July 20, 1908.

Physical examination revealed the following positive findings: Spine normal to inspection and normally flexible. Over the upper end of the sacrum and the fifth lumbar vertebra is an almost inconspicuous swelling, due apparently to a small accumulation of fat; it has no distinct boundaries, but extends almost to the sacro-iliac joints. It is asymmetrical in depth, being thickest on the right side. The back is covered with light colored lanugo, but over the left side of this lipoma there is a small tuft of very small, short, black hairs, about a dozen in number, about 1 cm. in length, and very slender. The lumbar spinous processes are easily palpable and appear well formed except the fifth, which feels small and lies a trifle to the right of the line through the others. Just below the fifth lumbar process, viz., at the site of the above-mentioned swelling, the fingers on deep pressure sink into a shallow depression, and bony contact is not transmitted. The rest of the sacrum and the coccyx appear normal to palpation.

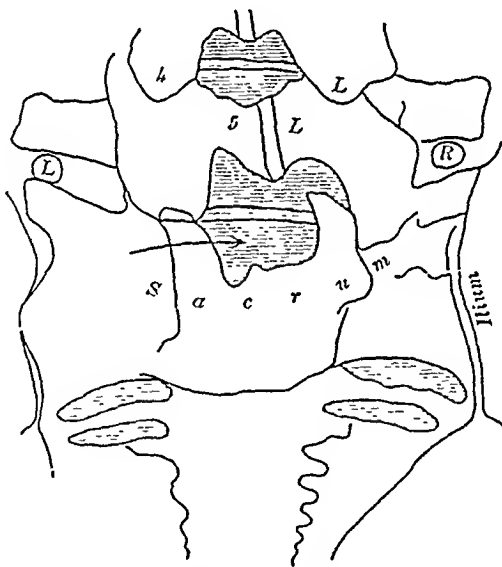
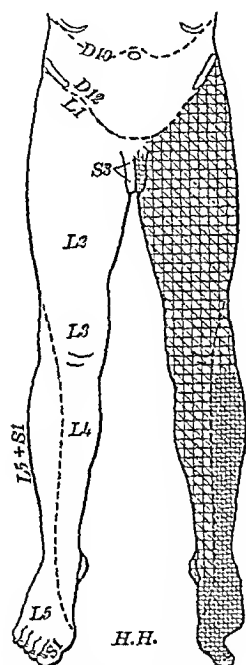


FIG. 9.—Helen H. Tracing of roentgenogram of spina bifida.

There is a sacrococcygeal dimple, but no sinus. Roentgenogram shows the spina bifida illustrated in Fig. 9. It consists of a distinct and extensive hiatus in the first sacral arch, most marked on the left side. The fifth lumbar arch is complete, but it is asymmetrical and narrow, the spine lying to the right of the midline.

The lower extremities show an atrophy of the left calf and exaggeration of the left knee-jerk. No ankle-clonus on either side. The outer side of the single remaining toe of the left foot is practically

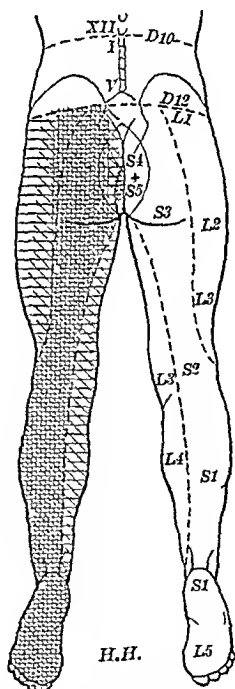
denuded of epithelium from a recent bleb. There is a plantar callus over the head of the second metatarsal. Scars of ulcers on the calf and over the tendo Achillis. Locomotion and station normal. Abdominal reflexes lively and equal. The right lower extremity shows no disturbances of sensation. The left lower extremity and left side of the anogenital region show the sensory paralyzes illustrated in Figs. 10 and 11, indicating, with the trophic disturbances, an involvement of the fifth lumbar and all the sacral nerve roots or segments on that side and a slight involvement of the second, third, and fourth lumbar roots.



\\\ Hypesthesia, tactile  
 ||| Hypesthesia, thermal  
 --- Hypalgesia  
 /// Anesthesia, tactile  
 |||| Anesthesia, thermal  
 ——— Analgesia

Anesthesia L5, S1, S3.  
 Hypesthesia L1, 2, 3, 4.

FIG. 10



Anesthesia-L5, S1, S2, S3, S4, S5  
 Hypesthesia-L1, L2, L3, L4

FIG. 11

Operation (Elsberg and Brickner), July 27, 1908. Slightly oblique transverse incision across the upper level of the sacrum carried down through the underlying fat, unencapsulated and finely lobulated, to the lumbar aponeurosis. Over the upper end of the sacrum this aponeurosis was found to dip in somewhat like a shallow funnel, but

there was no opening in it and no structure passed through it. The depressed portion of the aponeurosis was circumscribed, and this was dissected up from the underlying muscle, which was retracted, exposing a mass of fat and connective tissue extending down between the muscles in the midline and firmly attached to the under surface of the lumbar aponeurosis. No dura or congenital band was here encountered, but further dissection showed that the mass of fat and connective tissue stretched down to the pulsating dura mater seen through the large defect in the first sacral arch. This mass was dissected from the dura at the point where it found attachment. The dura was found to be not adherent to the overlying laminae in the neighborhood of the hiatus. The dura was then incised, cerebrospinal fluid escaping. Within the dural opening several nerve roots were seen floating in the fluid, some lying against the inner surface of the dura, but it was demonstrated that they were not attached to it. The dura was sutured and the hiatus was closed by a plastic operation.

Microscopic examination of the removed mass of fat, connective tissue, and aponeurosis showed no other structures within it.

The patient vomited and had headaches for several days after the operation, and required catheterization. Primary union. Involuntary urination developed for a few days and transitory diarrhea recurred.

Sensory examination a few weeks after the operation showed some improvement in the left lower extremity, as indicated in Figs. 12 and 13. She was discharged August 22, 1908. During the next few months she complained much of pain in the back. The pains in the left leg had, however, gradually diminished.

In October, 1908, there developed a plantar ulcer surrounded by callus, which healed very slowly. During the next few months she complained much of severe pains in the left groin and the back. During the following year recurrence of ulcers in the sole of the foot and calf, always preceded and accompanied by fever.

Operation (Elsberg and Brickner), May 16, 1910. Lumbar laminectomy—first, second, and third lumbar laminae removed. Dura opened and the exposed cord revealed the following: Its arteries were more prominent than normal. Much of the pia was lifted from the cord by coagulated cerebrospinal fluid. The cord proper extended farther down than usual, namely, to the third lumbar arch. The coagulated fluid was liberated, but no further lesion was noted in the cord or its roots, anterior or posterior, at this level. Laminectomy then continued down to the spina bifida, removing the fourth and fifth lumbar arches. There was then revealed at about the level of the fifth lumbar arch what appeared to be a lipoma of the cauda equina, occupying all of the spinal canal at this situation. It was soft, yellow, and of irregular conformation. Small pieces were removed for histological study, but it was impos-



sible to dissect the fat from the roots of the cauda equina, which ran through it and were intimately attached to it. The posterior fifth lumbar nerve root on the left side was then divided to relieve pain. Histological examination of this fatty tissue showed that it was a fibromyolipoma and contained a number of fine nerve bundles, some of which were apparently ramifications of larger nerves lying in the connective tissue. Most of the nerve bundles showed proliferation of the endo- and perineurium, and some of those lying in the fat were almost completely converted into fibrous cords. The connective tissue was rich in capillaries and arterioles, in most of which there were leukocytes, with perivascular aggregation of white cells. Some of the scattered striated muscle fibers showed degeneration. (Examination by Dr. I. Strauss.)

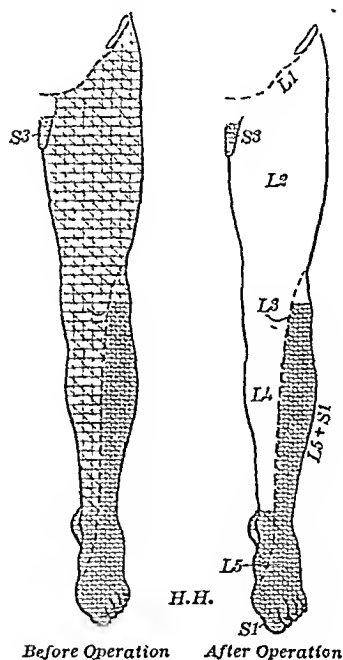


FIG. 12

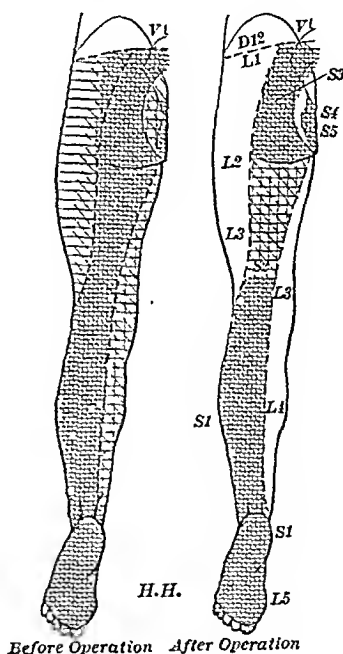


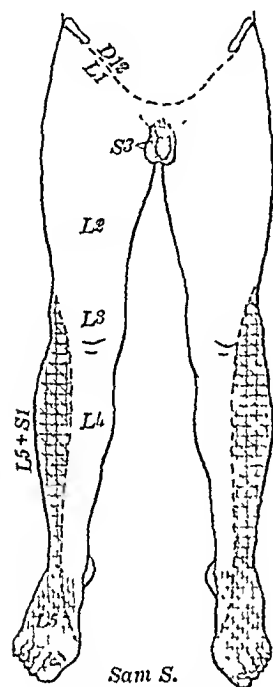
FIG. 13

Since this operation the patient's symptoms have progressed. A few months after it she developed drop-foot on the left side and subsequently also on the right side. She has very poor control of the bladder or rectum, complains much of backache, has cystitis from time to time, has frequent attacks of mucous colitis and frequent recurrences of the ulcerations. She walks but little, and out of the house is obliged to use a wheel chair.

These two cases are especially interesting in the laterality of the bifidity and, for a long period of years, of the symptoms. *They are interesting also in developing the observations concerning the*

growth of callus as a purely trophic phenomenon independent of pressure, and the prostration and marked rise of temperature which preceded and accompanied the outbreak of an ulceration, as we repeatedly noted.

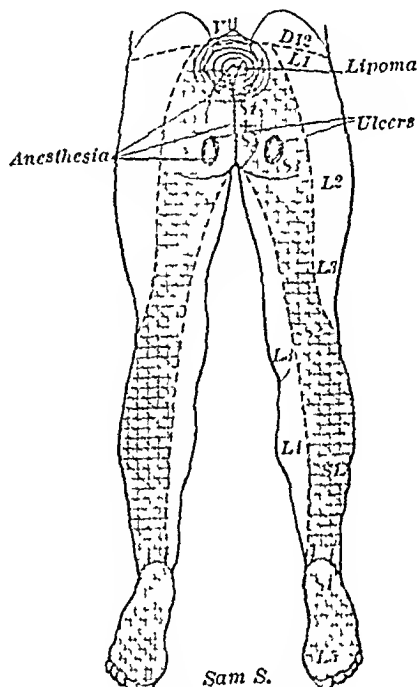
Sam. S., male, aged thirty years, suspender-maker, was admitted to the dermatological service at Mount Sinai Hospital July 15, 1915, with an ulceration, about two inches by three inches in extent, on each buttock, symmetrically situated two and a half inches from



Sam. S.  
Before Operation

Thermal Hypesthesia  
Hypalgesia  
Tactile Hypesthesia

FIG. 14



Sam. S.  
Before Operation

Thermal Hypesthesia  
Hypalgesia  
Tactile Hypesthesia

FIG. 15

the anus. These punched-out, freely discharging ulcerations had healed and recurred three or more times in a period of two years. The patient also had a purulent cystitis, of unknown origin, a right inguinal hernia, a peculiar falsetto voice, and a lipoma over the lumbosacral area characteristic of spina bifida occulta. He had no motor or rectal symptoms, but there was symmetrical sensory paralysis of the anoserotal regions, buttocks, and lower extremities, as shown in Figs. 14 and 15. No alteration of the reflexes. Wassermann reaction negative.

A roentgenogram showed a narrow cleft in the fifth lumbar arch and an absence of all the sacral arches (Fig. 16).

Under local treatment in bed the ulcerations healed and the patient was discharged, under observation, August 27, 1915.

When he reported again, ten days later, the ulcerations had recurred as before. He was then referred to me for operation and admitted to Dr. Elsborg's service.



FIG. 16.—Sam S. Roentgenogram showing cleft in L5 arch and wide hiatus in all the sacral arches.

Operation (Brickner), September 10, 1915. Semicircular incision over the upper and left border of the mass, a baseball-sized flattened lipoma, characteristically congenital in its fine lobulation and absence of capsule. It was cautiously dissected out. The wide sacral dehiscence was found covered throughout with a dense aponeurosis except at its upper end, where a small sac protruded into the surrounding fat, to which it was adherent. This sac was found to contain a few nerve roots so adherent to its inner surface that they could not safely be dissected from it. The herniated mass was a little larger than a thimble and escaped through a finger-tip-sized opening in the spinal canal. Below this opening the aponeurosis was incised to permit exploration. Only fat was seen, extra- and intradurally. Some of this was removed. The protruding nerve roots and attached dura were reduced into the canal *en bloc* and the opening was closed over firmly by a plastic operation on the aponeurosis.

Nine days later the wound was healed *per primam*, the ulcers were almost healed, and there was a decided improvement in the sensory disturbances. This improvement has continued (Figs. 17 and 18), and today practically nothing remains of the sensory paralysis—formerly so marked in the anogenital and gluteal regions—except thermal hypesthesia of the feet. I operated upon this patient a year ago for his inguinal hernia, and I have kept him under observation since the spinal operation two years ago, during which time the buttocks have remained solidly healed. Six months ago he had an infected abrasion of the dorsum of the right foot, but it healed normally.

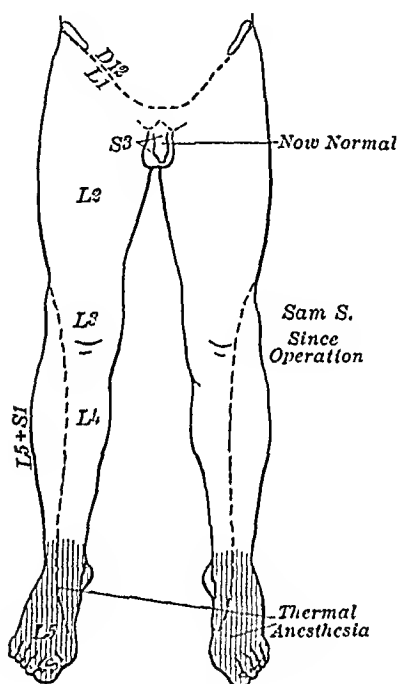


FIG. 17

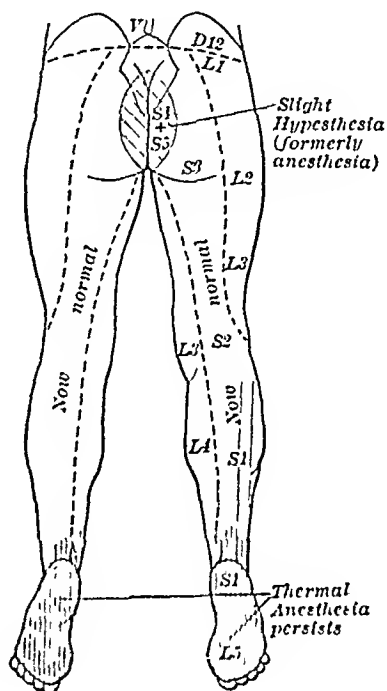


FIG. 18

Even if the continued cure of the previously recurring ulcers is a mere coincidence—which I cannot admit—the pronounced change in the sensory phenomena bespeaks a real benefit from his spinal operation.

GROUP II. *Spina Bifida Occulta, with External Signs, without Symptoms.* It would seem probable, especially from a study of the literature of abnormal hair growths, that some individuals with spina bifida occulta, even though marked by a very decided hypertrichosis or a congenital lipoma, go through life without any symptoms, or, at any rate, without any symptoms that bring them to the physician's attention. The following is such a case, although the patient died before he was twenty-three years of age.

Harold H., male, aged twenty-one years, was referred to me by Dr. Bullowa, and was in Dr. Elsberg's service at Mount Sinai Hospital in 1914 with a chondrosarcoma of the head of the tibia. Resection of the knee (Brickner), recurrence, amputation of thigh (Brickner). Intrathoracic metastasis. Died at Roosevelt Hospital, November 18, 1915. No motor, trophic, or sensory disturbances were noted, but he had a localized, bushy growth of long, straight hairs over the lumbosacral region (Fig. 19), and a roentgenogram showed a wide cleft in the fifth lumbar arch and a wide hiatus in the first, second, third, and fourth sacral arches (Fig. 20).



FIG. 19.—Harold H. Hypertrichosis over spina bifida occulta.

R. S., female infant, aged three months, admitted to Dr. Moschowitz's service at Mount Sinai Hospital August 18, 1916, with a congenital lipoma over the lumbar spine, small at birth but gradually increasing in size to that of a large crab-apple. No defect in the vertebral arches could be felt through it, and pressure upon it caused no symptoms. Physical examination otherwise negative.

August 22. Operation for spina bifida occulta lumbosacralis (Brickner). The swelling was partly circumcised and the lipoma, finely lobulated and non-encapsulated, was cautiously dissected up. A cleft was palpated in two arches, probably L5 and S1, closed over

by a tough membrane (*membrana reuniens*) except at one spot, through which fat extending from within the vertebral canal became continuous with the extravertebral lipoma. The membrane was incised to permit exploration, exposing much white fat lying upon and among the posterior roots of the cauda equina, which appeared normal. Much of this fat was picked out and the herniated portion

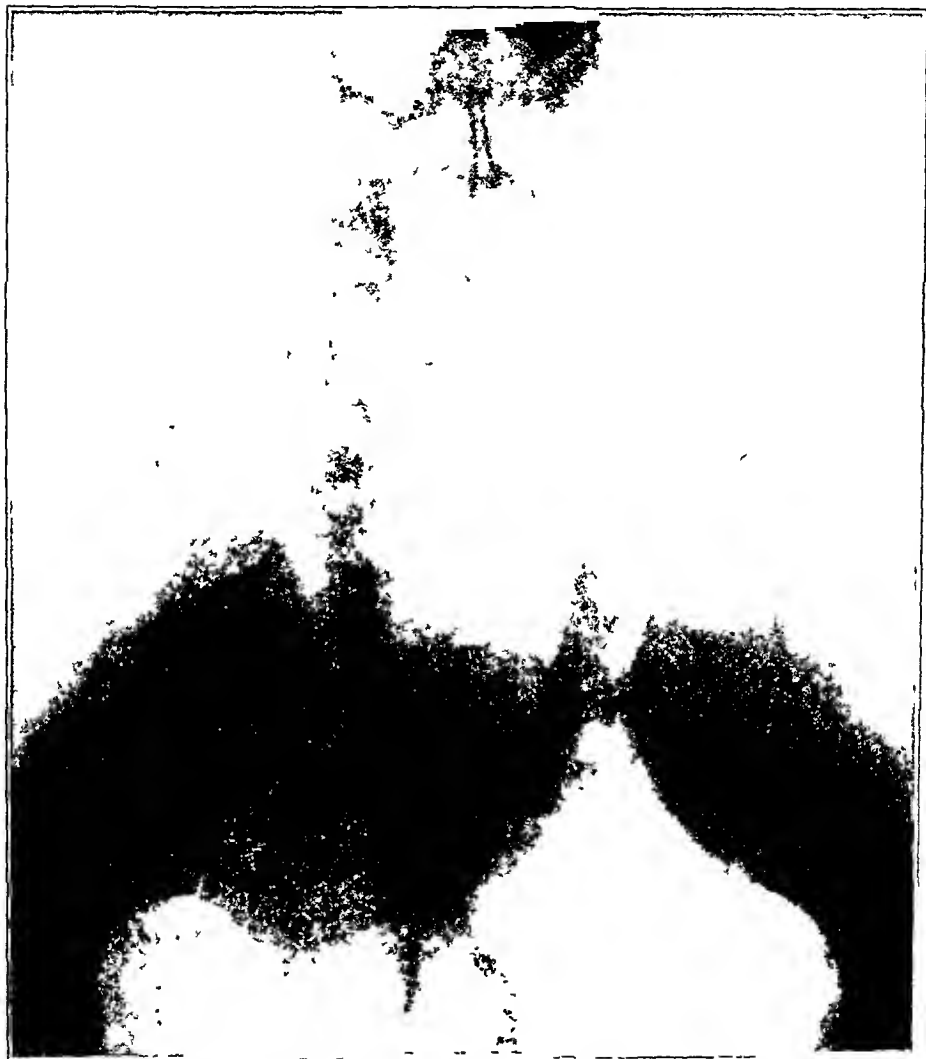


FIG. 20.—Harold H. Narrow cleft in L5 arch and wide hiatus in (almost complete absence of) S1 arch.

was removed. The membrane was closed with sutures, and a plastic closure of the lumbar aponeurosis was made over this. The baby was discharged, well, September 15.

Although the infant had had no symptoms the operation was done as a means of preventing, if possible, the development of symptoms later in life.

GROUP III. *Spina Bifida Occulta, without External Signs, with Symptoms.* This is the group to which I especially call attention, for it has hitherto scarcely been described.

In April, 1909, when I demonstrated before the surgical section of the New York Academy of Medicine the first and second cases here reported, the almost insignificant lipoma in the second case led me to conclude by urging "a careful scrutiny of the back and an x-ray picture in all cases in which there are incontinence of urine or feces or, in the lower extremities motor, sensory, or trophic disturbances, the cause of which is not otherwise evident."<sup>6</sup> I find that in the same year, 1909, Alfred Fuchs<sup>7</sup> published a study of 24 cases of enuresis in adolescents and adults, in which he described the following conditions, variously associated, as due to a congenital lower cord lesion which he called "myelodysplasia:" (1) Sphincter weakness, especially the so-called neurosis, enuresis nocturna. (2) Well-developed syndactyly between the second and third toes, and sometimes the fourth toe, in 66 per cent. of the cases. (3) Dissociated sensory disturbances in the feet, especially the toes, but also at the outer side of the feet, and chiefly thermal hypesthesia or anesthesia, in 75 per cent. (4) Defect in the sacral canal varying from an abnormally high opening of the hiatus sacralis to a spina bifida. Fuchs found these vertebral anomalies roentgenographically in 6 out of 10 cases of enuresis, and regards them as a rudimentary spina bifida occulta development. (5) Disturbances of skin and tendon reflexes, 11 of the 24 cases. (6) Foot deformities—percentage not stated.

Georg Peritz<sup>8</sup> agrees with Fuchs that the association of enuresis and spina bifida occulta sacralis is not merely accidental, thus disagreeing with Tromner and also with Lewandowsky, who, in his *Handbuch der Neurologie*, says that enuresis and spina bifida occulta are on the same degenerative basis, but have nothing to do with each other. In 22 adolescent cases of enuresis Peritz found spina bifida occulta roentgenographically in 68.2 per cent. In 20 children with enuresis Peritz found spina bifida occulta roentgenographically in 35 per cent.

William G. Spiller<sup>9</sup> reported a case of enuresis increasing, and motor weakness and sensory disturbances developing, after moderate exercise, in the lower extremities, in which the roentgenogram showed a grave defect of the sacrum and lower lumbar vertebræ, the back appearing entirely normal to sight and palpation.

Palmer Findley<sup>10</sup> renews attention to the fact that "virginal prolapse of the uterus occurs with greatest frequency in the newborn, and in most instances there are associated congenital deformities, notably spina bifida," and indicates that it would appear to be also a contributing factor sometimes in prolapse of the uterus in multiparous women.

In 17 cases of congenital prolapse of the uterus Ebeler and

Duncker<sup>11</sup> record that 15 had spina bifida; and they found occult spina bifida roentgenographically in 23 out of 28 multiparous women with prolapsus uteri. They also found it in 3 of 28 multiparous women without prolapsus.

The following 3 cases may be cited to illustrate this group. Palpation may or may not give sufficient indication of spinal arch deformity or dehiscence. Roentgenography shows it clearly.

Mollie C., unmarried, female, aged twenty-one years, was referred to me by Dr. Leon Lesser in December, 1915, for a partial incontinence of bladder and rectum, which existed since she was nine years old. She talked when one year old but did not walk until four. When in the street she often soils herself with urine or feces; at home she is able to reach the toilet in time to prevent this mishap. Her chief complaint is that she therefore must remain indoors most of the time. She urinates five or six times daily and once or twice during the night. Usually she has no diarrhea.

There were no other symptoms. The urine was normal. Physical examination was entirely negative. I found no sensory, trophic or motor disturbances and no abnormality of the reflexes. Nevertheless it occurred to me as possible that, in spite of the absence of any external sign, there might be an occult spina bifida. (I was not then familiar with the articles of Fuchs and of Peritz.) A radiogram showed a cleft in the third and fourth sacral arches (Fig. 21).

I had the girl admitted to Dr. Elsberg's service at Mount Sinai Hospital, where he and I observed her for a week, but no new data were developed. Cystoscopic examination showed no bladder lesion. In this case the limited character of the symptoms did not appear to urge the desirability of a spinal exploration. There is obviously no hernia of the cauda equina. The lesion is perhaps in the cord itself. Her condition has not improved during the past year and a half, however, and perhaps an exposure of the cauda equina may reveal some roots adherent to the membrane across the cleft, the release of which may be beneficial.

Benjamin T., male, aged fifty-eight years, was admitted to Dr. Moschcowitz's service at Mount Sinai Hospital June 3, 1916.

Twenty-five or more years before he developed a plantar ulcer of the left foot—an infected wound arising, he thought, from a shoe-nail. The foot became much swollen and the ulceration remained unhealed for several years. The infection gradually involved the first phalanx of the great toe, which was removed. Two weeks later the fourth toe became involved and the first and second phalanges were removed. Over the finally healed plantar sore callus formed, which the patient frequently pared down. For thirteen years the foot remained healed. Then a perforating ulcer reappeared at the same plantar site, and was finally healed. It



recurred four years later and persisted again for a long time before healing was effected, after treatment at the Vanderbilt Clinic and Har Moriah Hospital. Six months later it again recurred and involved the third toe, which was removed by Dr. Moschowitz. This was followed by healing.

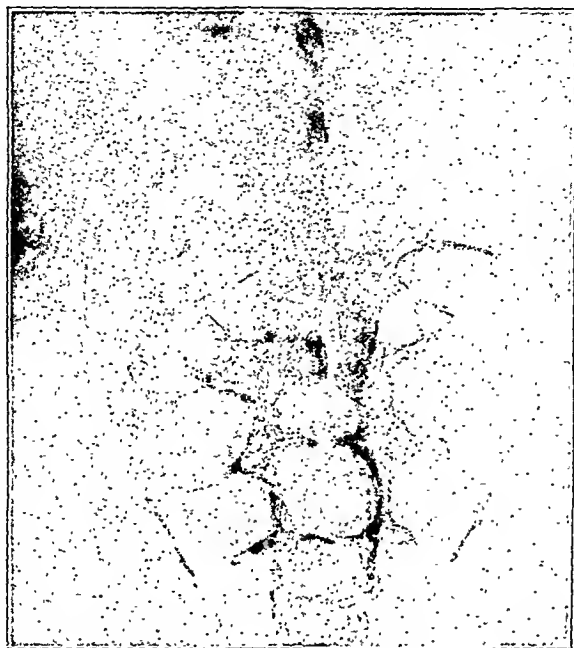


FIG. 21.—Mollie C. Sacral spina bifida occulta. Narrow clefts in the S3 and S4 arches.

Three months before admission to the hospital a painless blister, then an ulcer, appeared on the second toe, increased in size and depth, and extended into the metatarsophalangeal joint. The ulcer was the size of a dime, with sharp borders. The toe and the corresponding metatarsal region were dull red and swollen. There was slight tenderness. In a callous area over the ball of the foot was a linear scar 2 inches long. The fifth toe appeared normal; the first and the fourth had only the terminal phalanx; the third toe was missing; the second has been described.

The appearance was not that of arterial disease. The dorsalis pedis and posterior tibial pulsated normally on both sides. There was no "blushing" or "paling" phenomenon. The urine and heart were normal. Wassermann reaction negative. Blood-pressure 150 to 170. Emphysema. Gait and station normal. No bladder, rectal, or motor symptoms. The neurologist reported "a negative neurological examination. The condition does not depend upon any neurological disturbance."

It seemed to both Dr. Moschcowitz and me, however, that the phenomena were trophic in origin, and I suggested a roentgenographic examination of the lower spine for a bifidity. The sacral spinous processes were not palpable. Indeed, there appeared to be a depression involving the lower half of the sacrum. The roentgenogram showed an extensive sacral hiatus (Fig. 22). There is, in fact, thermal hypesthesia of both feet, although no apparent tactile hypesthesia or hypalgesia.

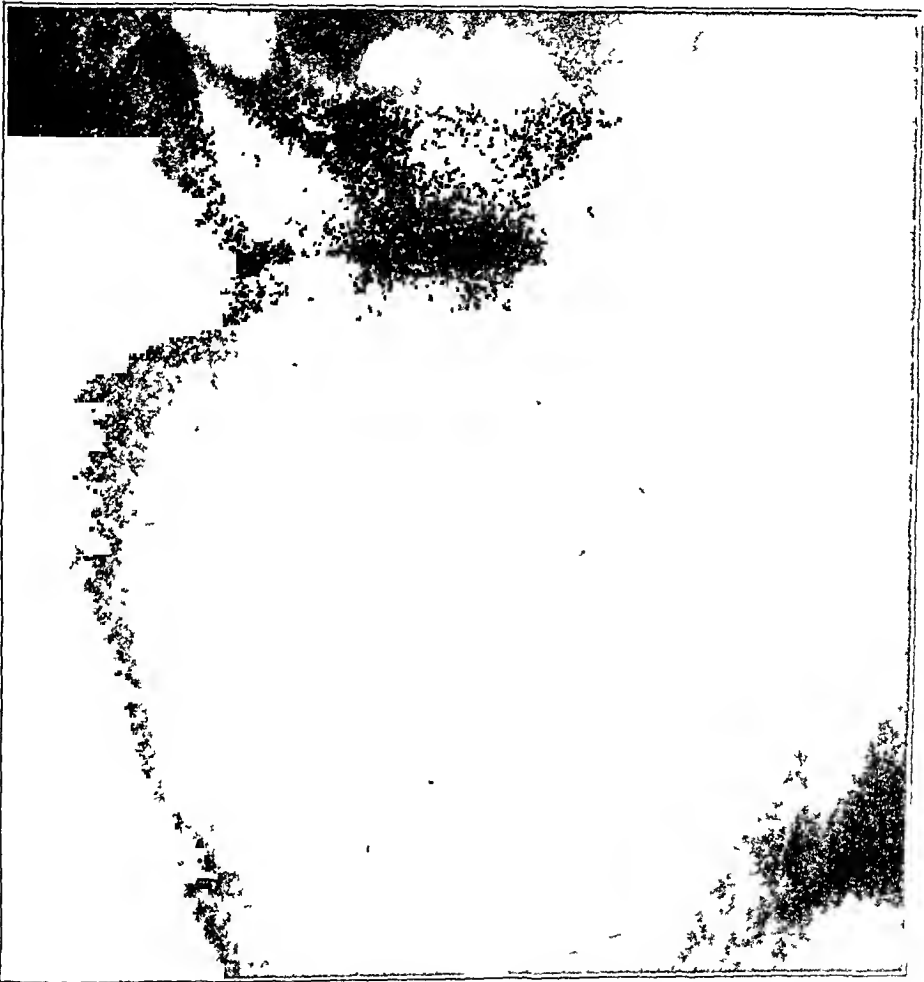


FIG. 22.—Benjamin T. Extensive sacral hiatus.

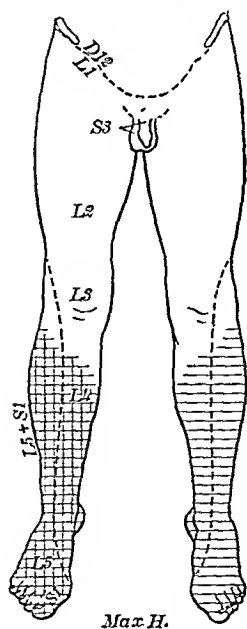
The third toe was amputated. With the healing of this wound there were no further symptoms and an exploration of the spine was considered unjustified. The patient is, however, under observation.

The following case I present quite tentatively, for the diagnosis is doubtful.

Max H., male, aged fifty-two years, on the neurological service of Dr. Sachs at Mount Sinai Hospital, January 17 to February



FIG. 23.—Max H. Symmetrical ulcerations of feet.



|||| Hypalgesia  
 |||| Thermal Hypesthesia

FIG. 24

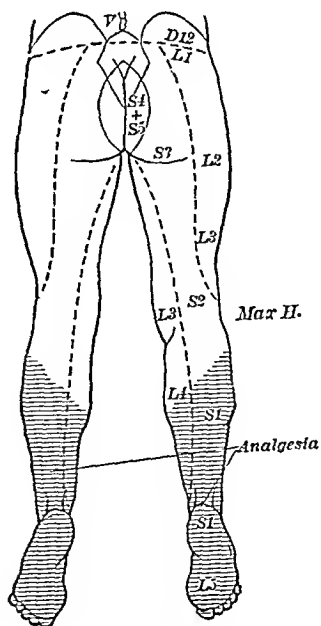


FIG. 25

24, 1917. Ten weeks before admission he had burning in the feet radiating into the legs, sometimes with tingling sensations in the finger-tips. Four weeks later ulcers developed on the feet, painless, and not tender. For some time he had been urinating very frequently, every half-hour during the day and twice at night; no shooting pains or trouble in walking.



FIG. 26.—Max H. Extensive sacral hiatus.

Examination gave the following positive findings: Hands cyanosed, cold and clammy; coarse tremor. The feet are cold, slightly cyanotic, perspiring. They show the following symmetrical ulcerations (Fig. 23): On each heel an area of dry gangrene about the size of a quarter; on the inner aspect of each big toe a gangrenous area the size of a dime; the right big toe shows also a gangrenous area the size of a nickel. There is ulceration about the nails of the second and third toes of the right foot. Pulsation of the dorsalis pedis artery is readily palpable in both feet. Hypalgesia and

analgesia are noted in both extremities, as shown in Figs. 24 and 25. Cerebrospinal fluid: 11 cells, 32 per cent. lymphocytes, 68 per cent. polynuclears; Wassermann reaction negative. Urine negative. Roentgenogram shows extensive sacral hiatus involving all of the arches except the first (Fig. 26). Electrical reactions normal.

The neurologists inclined to the diagnosis of a neoplasm either just above the conus or in the cauda equina. Dr. Sachs made the following note in the history: "Differential diagnosis between spinal gliosis with possible cavity and a neoplasm of the cauda equina. The onset thirteen weeks ago with sensory phenomena, rapid ulcer formation with gangrene, with preservation of gross muscular power and absence of marked vesical symptoms, argues in favor of neoplasm rather than gliosis. Even if gliosis were the condition, exploratory operation is advisable." Dr. Abrahamson believed that the lesion is a tumor of the type found in spina bifida occulta. Dr. Strauss seemed more inclined to think that the spinal bifidity is an accidental association and that the lesion is a cord tumor just above the conus.

February 17. The patient had a hemoptysis and developed dulness at the right apex. About the same time it was noticed also that there was diminished power in the right lower extremity. He refused operation and left the hospital unrelieved.

None of my 3 cases of spina bifida occulta without external signs with symptoms, and none of the cases of enuresis, etc., recorded by Fuchs, Peritz, Spiller (and one by Alfred Sanger<sup>12</sup>), has been submitted to operation, and a lesion of the cord structures corresponding in type to a spina bifida has therefore not been demonstrated.

Admittedly in some cases at least the bifidity of the spine may be a congenital abnormality that has no etiological relationship with the symptoms, but in many cases, and especially in the case of Benjamin T., with the fairly characteristic progressive ulceration of the toes of one foot and the thermal hypesthesia of both feet, the presumption is very strong that the lesion at fault is indeed a spina bifida occulta.

GROUP IV. *Spina Bifida Occulta, without External Signs, without Symptoms.* For some years I have been interested in observing that a considerable number of roentgenograms of the lower spine of patients exposed for examination of the urinary tract, the hip, etc., shows a cleft most often in the fifth lumbar arch or in one or more of the sacral arches. In what percentage of apparently normal individuals this anomaly is found roentgenographically I cannot say, but I have the distinct impression that it is not very uncommon. Perhaps a careful inquiry into some of these cases might show some disturbance of bladder control or loss of thermal or tactile sensitiveness in the lower extremities; but in the absence

of such a study I think we may be prepared to believe that there is found in a certain proportion of healthy individuals a congenital defect in the lumbar or sacral arches without any affection of the spinal cord tissues. The following cases are illustrative.



FIG. 27.—George K. Asymmetry of L5 arch, cleft in S1 arch, wide defect in lower sacral arches.

The first is that of a spina bifida occulta involving the first and the lower sacral arches (Fig. 27), probably not associated with the symptoms:

George K., aged forty-six years, was in the neurological service of Mount Sinai Hospital January 17 to January 31, 1917, with aeroparesthesia of the hands and feet.

Following a fall on his back he had suffered for ten years with radiating pains in the lower extremities, varying with the weather. For ten months he had continuous burning pain in the tongue, hands and feet. His hands and feet swelled when dependent.

He had paresthesia ("pins and needles") in the feet. For five years he had impotence and prostatorrhea.

There was decided hyperesthesia of the legs, anteriorly and the buttocks. Tendon reflexes of all four extremities much exaggerated. Lumbar puncture—normal cerebrospinal fluid. Slight polycythemia. Palpation of the sacrum suggests an absence of the lower spinous processes. Other data negative. Roentgenogram shows a spina bifida occulta, illustrated in Fig. 27.

The following case is interesting in the differential diagnosis of the ulceration and gangrene of the toes, the peculiar anomaly of the lower vertebral arches, and in the operative finding:

Isidore B., Russian, male, aged twenty-eight years, was admitted to Dr. Beer's service at Mount Sinai Hospital in August, 1916, with moist gangrene of the fourth and fifth toes of the right foot and mild cellulitis of the anterior portion of the foot. For two years there had been progressive infection, ulceration, and gangrene of the third, second, and first toes of this foot, with failure of the stumps to heal and extension of the process to the plantar surface. The involvement of the fourth and fifth toes had begun three months before admission. During all this time he suffered *severe pain*, which is characteristic of thrombo-angiitis and not of the trophic gangrene of spina bifida.

On the left side the dorsalis pedis and posterior tibial arteries pulsated well, but on the affected side no pulse could be felt in either vessel. The superficial and deep reflexes of all extremities were exaggerated, especially in the lower extremities. No sensory disturbances were elicited. Wassermann reaction negative.

Dr. Abrahamson noted a superficial cleft in the tips of the spinous processes of the eleventh and twelfth dorsal and first and second lumbar vertebræ. A roentgenogram revealed the peculiar deformity of the fifth lumbar and first sacral arches shown in Fig. 28. Although there is no actual cleft in any arch, this type of lamina malformation is seen, as I have shown, in other cases with bifidity; it produces a distinct hiatus vertically, and I think the abnormality may be properly grouped with spina bifida occulta.

Although the patient's disease was fairly diagnosticable as a thrombo-angiitis obliterans, it seemed worth while to give him the benefit of a doubt suggested by the vertebral deformity and to explore it for a possible cauda equina lesion. Dr. Buerger kindly transferred the patient to my care for that purpose.

Operation (Brickner) September 8, 1916. The fifth lumbar and first sacral arches were exposed and found abnormally separated. They were removed, the dura was incised, and the cauda equina was exposed in its bed of fat. It presented no gross lesion. The dura appeared in all respects normal. Spinal fluid escaped under great pressure.

The wound healed *per primam*, and after the operation there was a remission in the subjective symptoms. The second toe was

amputated September 19. There has been a progression of the disease, and the foot will probably require amputation.

The amputated toe showed "chronic suppurative inflammation, granulation tissue, and endarteritis. A diagnosis of primary arterial lesion cannot be determined from the specimen" (Buerger).



FIG. 28.—Isidore B. Malformation of L5 and S1 arches producing a longitudinal hiatus.

Taken all together, the results of operation for spina bifida occulta are not brilliant, and probably for the reason that the degenerative and neoplastic processes are scarcely remediable. Those cases in which there is a hernia of the spinal roots probably offer the best chance for a good result; for the reduction of this hernia into the bony canal, by relieving the contained nerve roots of traction and pressure, may greatly improve the existing symptoms or prevent the development of some others. The third case, Sam S., the young man with the trophic ulcers of the buttocks, represents, I think, a highly satisfactory result from such an operation. Even when there is no meningocele much may be found possible at operation—for example, separation of adherent nerve roots from the membrana reunions, division of a constricting band, removal



of an endostosis, or *perhaps* even the removal of a teratoma of the cauda equina.

I believe that the following are legitimate indications for operation:

1. In infants and children, spina bifida occulta with congenital lipoma or hypertrichosis, even though without any symptoms—to reduce the spinal hernia into the canal or to meet any other indication that is found, in the hope of *obviating* the development of symptoms during adolescence. The case of the infant that I have reported is illustrative of this indication.

2. In adults, spina bifida occulta with sufficiently serious and especially with progressive symptoms, and this I believe should apply whether or not the spina bifida occulta is marked by external signs (lipoma, hypertrichosis). I am not unmindful of the inherent risks of such an operation, but surely progressive gangrene of the lower extremities and incontinence of the sphincters are indications sufficient to justify the taking of such risks. In the literature I have found records of 12 operations. I am adding now 5 to these—all of the 17 without mortality, and some with decided benefit. In all 5 operations for spina bifida occulta within my personal experience there was no untoward result, and the wounds in all cases healed *per primam* and without any spinal infection.

In making this presentation of a condition that has for so many years interested me, it has been my purpose to call attention to the four groups into which it seems to me we may clinically divide spina bifida occulta, and to suggest the advisability of a roentgenographic examination for such a condition in all cases of sphincteric, sensory, trophic, or motor disturbances that might thus be explained, even though there is no external manifestation to suggest its presence.

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## DIATAXIA CEREBRALIS INFANTILIS: THE ATAXIC TYPE OF CEREBRAL BIRTH PALSY.\*

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THE classification of the cerebral palsies of early life has engaged the attention of neurologists and psychiatrists for a number of years. A great many clinical types have been described, and in recent years there has been considerable progress in our knowledge of their various causes and underlying pathological changes. The subject, however, still presents many obscurities in etiology, localization and symptomatology.

The cases have been variously grouped in accordance with the etiology, the nature of the pathological changes or the clinical symptoms presented. For all practical purposes the clinical classification is the important one and the most useful, as post-mortem examination and histological study are usually necessary to determine the true pathology of any case and the original causative factors are often obscure and difficult to determine. This is especially true of the congenital cerebral defects and malformations resulting from disease of the fetus during the period of intra-uterine life.

The common clinical type of infantile cerebral palsy is the spastic form. This may appear as hemiplegia, paraplegia or triplegia, and very frequently as a cerebral diplegia. It is characterized by paralysis with various spastic phenomena, either alone or in association with other cerebral symptoms, such as choreiform manifestations, ataxia, tremor, athetosis, mental defect, epilepsy and disturbance of the special senses.

A classical description of this large clinical group and its relationship to injuries received at birth was given by an English physician, Dr. Little, in 1862. In recognition of this important contribution, those cases of *cerebral spastic paralysis* resulting from injury to the brain at birth are very commonly known under the generic title of Little's disease. Little's conception that certain abnormal types of parturition, especially those associated with difficult and prolonged labor, produced hemorrhages over the surface of the brain which interfered with the normal functions and development of motility has been upheld by many subsequent investigators. Prominent among these may be mentioned the names of Sarah McNutt, Freud, Gowers, Railton and Kundrat.

\* Presented at a meeting of the American Neurological Association held at Boston, May 23, 1917.

Little also pointed out the importance of premature birth as a cause of cerebral spastic paralysis, and some observers, notably Brissaud, would limit the term Little's disease to this comparatively small group of cases, in which the development of the pyramidal tracts has been checked or retarded by premature delivery. This limitation of Little's conception in the opinion of many writers is not justified, and a perusal of his original monograph will, I believe, convince most readers that the essential idea underlying his work was the relationship of all forms of abnormal birth to the cerebral spastic palsies of early life.

Förster, in 1909, described in some detail an unusual clinical type of cerebral diplegia which he termed the *atonic-astasic type* of infantile cerebral palsy. This group stands in striking contrast to the spastic type of Little, and is characterized by motor paralysis with flaccidity. There is inability to stand or walk (astasia-abasia), great difficulty in articulation, not infrequently mutism, and a marked mental defect. A certain degree of individual movement of the extremities is possible, but all the larger and more complicated motor activities are impossible, owing to a defective action of antagonistic and synergic groups of muscles. Slight spastic phenomena are sometimes noted in the lower extremities, but the essential quality of the paralysis is flaccid and atonic.

Many of the symptoms in this group of cases suggest a cerebellar origin, and Förster was at first inclined to attribute this origin to the symptomatology until later two of his cases subjected to postmortem examination revealed an extensive lobar sclerosis of the frontal region, the cerebellum appearing quite normal on macroscopic examination. Unfortunately, no microscopic studies were recorded.

A few years later, in 1913, Pierce Clark reported similar cases under the rather comprehensive title, "Cerebrocerebellar Diplegia of Flaccid Atonic Type," and concluded on purely clinical grounds that the lesion was probably a combined one, involving both the cerebrum and the cerebellum, notwithstanding the negative cerebellar findings in Förster's cases.

Clark assumed that a cerebellar lesion alone would be amply compensated for by the cerebrum if the cerebral structures were normal, and therefore a combination of cerebral and cerebellar symptoms as occurs in this group of cases would be in favor of a combined lesion of these two structures. Against this point of view, however, may be mentioned the normal appearance of the cerebellum in Förster's cases and also the fact that grave disturbances of muscle tone and coördination may result from lesions of the cerebral cortex. Accordingly, the term cerebrocerebellar diplegia in the present state of our knowledge would seem hardly justified and the simple clinical designation atonic or flaccid type of cerebral diplegia as used by Förster is, I believe, preferable.

Batten and von Wyss have also recorded examples of this flaccid type, and there can be no question as to its distinctive clinical characteristics and marked contrast to the spastic types of Little.

Under the title "Congenital Cerebellar Ataxia," Dr. Batten has described what he terms a pure *cerebellar type* of diplegia. This group is characterized by ataxia of the cerebellar type, which displays, however, a decided tendency toward recovery. There is little or no mental defect, and the clinical picture is one of pure ataxia of cerebellar origin involving speech, the gait and station and various movements of the extremities.

Therefore, according to our present classification, the cerebral diplegias of childhood may assume one or other of the following clinical forms; the *spastic* type of Little, the *atonic* or *flaccid* type of Förster and a *cerebellar* type as described by Batten. These may exist as such in pure form or may occur in various combinations. They may also present a variety of complications and associated symptoms such as epilepsy, mental defect, choreiform and athetoid manifestations, which give to this whole chapter a large and varied symptomatology.

The group of the cerebral diplegias to which I would direct attention as a distinct clinical variety is an *ataxic type of cerebral birth palsy*. The ataxia is bilateral in distribution and is characterized by a generalized disturbance of coördination involving the gait and station, the use of the arms and legs, and the muscles subserving the function of speech. The incoördination persists in the recumbent posture and has the characteristics of a true ataxia. It is, I believe, of cortical origin. There is neither paralysis nor spasticity, and the cases observed were free from serious mental defect or epilepsy. In the absence of any direct pathological evidence I would suggest, as the probable etiological factor, an injury to the fetal head received at birth, producing rupture or thrombosis of the cerebral veins, with limitation of the lesions to the cortex of the parietal lobes.

The clinical picture is one of pure *cerebral diataxia*, and may be regarded as the sensory equivalent of *cerebral diplegia*. In my opinion, however, the vascular lesion, instead of being limited to the motor area as in spastic diplegia, is situated more posteriorly behind the fissure of Rolando in the sensory sphere of the cortex, thus implicating the centers and commissural systems which are engaged in the reception and transmission of the memories of movement.

The parietal lobe is the great receptive center for the registration of sensory stimuli, representing movements and the various combinations of movement, and a bilateral lesion in this area would necessarily impair in greater or lesser degree the normal development of motility and coördination.

CASE I.—The patient, E. C., was a boy, aged twelve years, born of healthy parents. There was no history of any familial nervous or mental disease. With the exception of measles, chicken-pox and tonsillitis there was no history of any serious illness.

He was an only child, born at term, the labor being unusually difficult and prolonged. The mother stated that she was thirty-five years old at the time and was in labor for forty-eight hours. The membranes had ruptured early and delivery was eventually effected by forceps. The child was born blue and asphyxiated and did not cry for several days. There were general convulsive seizures during the first few days, but none subsequently. The head was said to have been out of shape and deformed, but gradually assumed a normal symmetry. An effort was made to feed the child by the breast, which was unsuccessful and had to be abandoned.

Very early in the child's life it was noted that the movements of the extremities and trunk were weak and awkward. Swallowing was performed without apparent difficulty; there was, however, a tendency to drooling, which persisted for several years. It was noted that the child did not sit up or show much tendency to creep until the end of the second year. The movements then were awkward, unsteady and accompanied by unusual efforts. Unsteadiness of the movements was noted quite early and has persisted up to the present time. Both sides were involved, but the right arm seemed to be more affected than the left, and the legs showed a greater degree of disability than the arms.

The child did not speak until the third year, and then only uttered inarticulate sounds. He has shown slight but steady improvement from year to year in speech, in his ability to sit or stand and in the use of the arms. He could not stand alone until the sixth year, and is still unable to walk alone.

The general health and intelligence are both good. The mother insists that the child is bright and learns readily. He is quite cleanly in his habits, and is able to control the sphincters. He is not able to feed himself or dress himself on account of the severe motor ataxia. He is good tempered, and is interested in the books and games suitable to his age. He has had no convulsions since the initial spasms after the birth, which lasted several days. The special senses are apparently not affected.

*Examination, May, 1916.* The boy is of good size, well nourished, and appears in excellent general health. The muscles are moderately well developed. There is a slight tendency to motor restlessness and atactiform movements unless supported and in a relaxed position. This unrest is increased by any action, however slight, and by mental excitement. There is no true chorea or athetosis, but the ataxic disturbance has a somewhat choreiform character when the motor agitation is extreme.

He is able to stand by holding on to a chair, but not unsupported. While standing in this position there are swaying, unsteady movements of the trunk and arms in the effort to maintain the equilibrium. The head also shows ataxic oscillations. On attempting to take a few steps, even with assistance, the ataxic disorder becomes extreme and he falls backward or to the side and has to be supported; occasionally the legs give way under him.

In testing the movements of the upper extremities a very marked incoördination is demonstrable. On attempting to carry the finger to the tip of the nose there are irregular atactiform movements of the extremity and compensatory or associated movements in other parts of the body—for example, the head and trunk. This disorder of motility does not resemble an intention tremor but is a gross disturbance of the power of coördination. It is especially well marked if an effort is made to grasp a small object or to draw a line with a pencil. Such movements are carried out in a brusque and awkward manner, and any breakable object would surely be sacrificed if he were allowed to reach for it. If the attempt is made to hold out the arms with the hands and fingers extended there are irregular atactiform movements and changes in the relative position of the extremities, which are somewhat increased by closure of the eyes.

The alternating rhythmical movements of the wrists or fingers, as a result of the ataxic disturbance, are impaired. Dysdiadochokinesis is therefore present.

In the recumbent posture the lower extremities show a similar atactiform disturbance. If the attempt is made to place the heel upon the opposite knee there is a marked incoördination and uncertainty of movement, as might be observed in an advanced case of spinal ataxia.

Similarly, if the legs and arms are elevated while lying flat on the back and the effort is made to fix them in this position the extremities are moved about in extreme incoördination, and frequently the balance is lost and he rolls over to one side. The right arm and leg showed a somewhat greater degree of involvement than the left, which coincided with the early history and observations of the mother.

There is no demonstrable weakness or paralysis of the limbs. Indeed, the gross motor power of the lower and upper extremities is well preserved, except as modified by the ataxia. There is no atrophy. There is not the slightest evidence of spasticity in either the upper or lower extremities. Instead, the tonus of the musculature is moderately diminished.

The knee-jerks are present, equal and not exaggerated. The Achilles-jerks are inactive and only elicited with difficulty. The supinator jerks are not elicitable. The biceps- and triceps-jerks are inactive and variable. There are no periosteal reflexes in either the

upper or lower extremities and no clonus or spastic phenomena. The abdominal, cremasteric and plantar reflexes are present and of normal intensity. The Babinski phenomenon is absent.

*The sensation*, both superficial and deep, is apparently undisturbed. Touch, pain and temperature are recognized promptly, and so far as could be determined were well localized. The deep sensibility also appears normal. Pressure of the muscle induces pain and the sense of position is preserved. He recognizes the direction of passive movements of the toes, fingers and of the larger joints, promptly and without error. The sense of vibration is acute.

The pupils are equal and react promptly to light and accommodation. The pupillary skin reflex is active.

There is no nystagmus and the optic nerves are normal. On attempting to fix an object with the eyes there are slight rolling movements of the eyeballs, apparently of an ataxic nature, and associated atactiform oscillations of the head. There is no paralysis of the cranial nerves. The tongue is protruded in the median line, the palate is promptly innervated and the movements of the jaw are normal in power and extent. Facial innervation is equal on the two sides.

There is a considerable degree of dysarthria, and it is rather difficult to understand the spoken words. The mother, however, interprets perfectly and can carry on a very intelligent conversation with the boy. He can name ordinary objects placed in the hands, and there is no astereognosis. Sight, hearing and smell are normal.

The heart and lungs are normal.

The urine is free from albumin and sugar. The Wassermann test of the blood is negative.

NOTE.—The above findings were confirmed at several subsequent examinations. The essential disturbance was one of incoördination without paralysis or evidences of spasticity, which affected nearly all voluntary movements. While in the recumbent posture, with the musculature relaxed, there were no evidences of chorea or athetosis. On making the effort to stand or walk, and in certain postures, there were incoördinate movements which suggested a choreiform tendency, which, however, appeared to be dependent upon the degree of the ataxic disturbance. The right side showed a greater degree of involvement than the left. The tonus of the muscles was moderately reduced. There was, however, no undue flexibility of the extremities as occurs in the higher grades of hypotonicity. The kneejerks were readily elicitable and not exaggerated. The Achillesjerks could usually be elicited, but with difficulty, the same being true of the reflexes of the upper extremities. The plantar reflex was always of the normal type, and a true Babinski reflex was not obtained.

So far as could be determined the general sensations, both superficial and deep, were well preserved.

CASE II.—The patient, L. H., was a girl, aged six and a half years. The family history was good and there was no tendency to hereditary or familial diseases. The parents were healthy and were not related. The mother had given birth to two other children without special difficulty, and there had been no miscarriages.

The patient was the third child and the pregnancy had progressed without untoward complications. The birth occurred at term and the labor was extremely slow and tedious. After twelve to fourteen hours a faulty presentation was discovered and the delivery was effected by means of forceps. The child was born asphyxiated, and it was feared at the time would not survive. Artificial respiration was necessary and the child did not cry or take the breast for about two weeks. After this she took the breast, but only with some difficulty, and the cry was weak and feeble. The subsequent development was slow and retarded. The child could not sit up until two years of age, and then was unsteady and swaying, often falling backward or to one side. About this time she was able to creep, but with difficulty. Movements of the arms and legs were awkward and unsteady. Attempts to stand were not successful until the third year, and then only by holding on with the hands and accompanied by swaying of the body and frequent falls. Attempts at walking were only possible in the latter part of the third year, and then required careful assistance, as falls were frequent and often severe.

At the age of three years the child could speak a few words, but indistinctly, and only the mother could understand them. Swallowing occurred without difficulty and the special senses were apparently normal. The child was bright and took an interest in her surroundings, but was backward as compared with other children at the same age. On attempting to grasp an object with the hand the movements were uncertain and awkward.

The child had shown decided but gradual improvement. She had acquired better control of her movements and articulation was more distinct. She was fairly intelligent for her age but still somewhat backward in many things, which the mother attributed to her physical disabilities. There was no history of convulsive seizures.

*Physical Examination October, 1914.* The child is well nourished and fairly well developed for her age. While sitting quietly in a chair the extremities and trunk are motionless. There is a slight tendency to swaying and oscillation of the head, especially with any movement, such as fixation of an object with the eyes or when speaking.

Any attempt to raise an arm or leg evokes awkward ataxic movements of an incoördinate character. On attempting to grasp an object with the hands there is a series of irregular, incoördinate movements; the fingers are overextended, the hand is thrown about in an awkward manner and the object is grasped brusquely. There is no weakness of the movement or of the grasp—it is a pure ataxia of movement or incoördination. The disturbance is about equal on the two sides.



The child understands spoken language and talks, but articulation is dysarthric and indistinct and accompanied by slight atactiform movements of the head and trunk, especially if standing. In standing there is manifested a distinct disturbance of equilibrium. She stands on a broad base, with swaying of the trunk and various compensatory movements of the arms. This static ataxia is increased slightly by closure of the eyes. On attempting to walk a definite disturbance of the gait immediately becomes apparent. There is unsteadiness of equilibrium, pitching to and fro and great uncertainty of movement. In appearance it suggests very strongly the titubating gait of cerebellar disease. The legs are held far apart, the head erect and the arms used to balance. The movements of the legs are awkward and ataxic. On attempting to stand quietly there is a slight choreic unrest, which, however, is ataxic in origin and is not noticeable in a quiet and relaxed position. The ataxia does not disappear in the recumbent position. For example, on attempting the finger-nose test or the heel-knee test, while flat on the back, the incoördination of movements is scarcely less marked than in the erect posture or sitting in a chair. There is no cessation or diminution of the ataxia when the recumbent posture is assumed. In this position, if the arms and legs are elevated, and the attempt made to hold all four extremities upright, with the eyes closed, incoördinate, ataxic movements persist with unabated vigor. If the hands and arms are held outstretched, while sitting in a chair there are ataxic movements of the upper extremities and some swaying movements of the trunk. Rhythmic alternating movements of the wrist and fingers are performed slowly and awkwardly. Evidences of dysdiadokokinesis are therefore present.

The cranial nerves are normal. The tongue is protruded in the median line, the facial innervation, movements of the soft palate and of the mandible are all normal. These movements are associated with slight atactiform manifestations of the head and trunk.

The optic nerves are normal. There is no nystagmus and the pupils are equal and react to light.

There is no paralysis and all movements show a normal degree of power. The muscles are well developed and show no atrophy.

There is no spasticity in either the arms or legs and no clonus. The tonus of the muscles is slightly reduced but the hypotonicity is of moderate degree. There is plantar flexion of the toes; the Babinski reflex is not present.

The knee-jerks are present, equal and of normal intensity. The Achilles-jerks are faint and at times not elicitable with certainty. The arm reflexes, supinator, biceps- and triceps-jerks, are inactive and not definitely elicitable. The abdominal reflexes are present.

General sensation was apparently normal. Touch, pain and temperature stimuli were correctly interpreted and, so far as could be determined, were well localized.

The deep sensibility and sense of posture were also preserved.

The child could recognize the movements of the toes whether up or down, but if the order was given to place the left limb in the same position as the right, either the arm or leg, the attempt was made and sustained awkwardly and in an uncertain manner, probably on account of the ataxia. Sight, hearing and smell were not affected. There was no astereognosis. Such common objects as a coin, pen-knife or a key were promptly recognized in either hand.

There was no special mental defect; the child was good natured, responsive and well behaved and was not far below the mental average for her age.

Heart and lungs were normal. Wassermann test of the blood was negative. Urine negative.

NOTE.—This case, like the preceding, presented symptoms of a pure ataxic disturbance which affected nearly all voluntary movements, such as standing, walking and the individual activities of the extremities. The gait was very suggestive of a cerebellar ataxia but both the upper and lower extremities showed a definite ataxia which persisted in the recumbent posture. Lying flat on the back, with no demands upon the function of equilibrium, it was impossible to hold the extremities quietly in an elevated position as in cases of pure cerebellar disease, the ataxic disturbance persisting as in a case of spinal ataxia. There was no demonstrable weakness of the extremities and no spasticity. The sensibility was normal. There was no true chorea, athetosis or intention tremor. The slight choreiform tendency did not suggest true chorea but resembled rather the choreic unrest which is sometimes present in cases of advanced Friedreich's ataxia. The disorder of motility was an inability to regulate and coördinate voluntary movement. The condition was manifested soon after birth and was characterized by steady improvement. There was therefore no tendency to progression or aggravation of symptoms.

CASE III.—The patient, A. H., a girl, aged eleven years, was the last of seven children. The circumstances attending the birth were abnormal, the membranes ruptured quite early and labor was unusually prolonged and severe. The child was eventually delivered with forceps in an asphyxiated condition and was resuscitated with difficulty. She was said to have been "blue" for several hours after birth and the imprint of the forceps remained over the temporal region for a week or more. She did not take the breast readily and was nourished by the bottle. During the early months of life she was restless and difficult to quiet, crying a great deal, and was physically frail.

It was soon observed that the motor development was not normal. Such acts as holding up the head, sitting and attempts to crawl and walk were all considerably delayed, as was also speech.

She was unable to stand before the sixth year and then only with

assistance. The movements of the arms were noted to be irregular and unsteady early in the second year and articulation was indistinct up to the fourth year, but has shown a steady improvement since that time.

With the exception of summer diarrhea and chicken-pox the child has had no illnesses of note. The other children of the family were in good health. The father died of pneumonia and no history of any neuropathic heredity could be elicited.

The mother states that while somewhat backward for her age the child is bright, has learned to read a little and is especially fond of music. The special senses were not affected. There has been a gradual improvement in the motor disability from year to year, especially in speaking and walking. There has been no history of any convulsive seizures, excepting immediately after the birth, when there was an indefinite history of several spasmodic attacks.

*Examination, November, 1912.* The patient is thin and somewhat pallid; the teeth are uneven and defective.

The skeletal development is rather slight and fragile. The muscles are well formed and, although small, are not atrophic. On attempting to rise from a sitting posture there is a very evident disturbance of gait and station. She stands on a broad base, the trunk swaying from side to side and balancing with the arms. After a few moments she becomes somewhat adjusted to the change of posture, but slight atactiform and balancing movements persist. Closure of the eyes increases somewhat the degree of static ataxia.

While walking there is apparent a marked disorder of movement. The legs are lifted and thrown out in an awkward, ataxic manner and there are numerous compensatory lurches and balancing movements of the head, trunk and arms. She is, however, able to walk alone and with a fair degree of security, and does not fall. While sitting in a relaxed posture in a chair the musculature is quiet, and only occasionally slight atactiform movements of the head or arms are observed. On attempting to stand or walk or on initiating any movement of the extremities a considerable degree of ataxia results which is somewhat choreiform in appearance, but occurs only as an accompaniment of movement.

There is a general condition of marked incoördination. On attempting to grasp an object with the hand or on placing a finger on the tip of the nose a considerable degree of ataxia of the arms is apparent, which is increased by the associated atactiform movements in other regions of the body, as, for example, the head and trunk. The two arms are about equally affected.

There is also marked retardation and awkwardness in performing alternating rhythmic movements of the wrist and fingers (dysdiadochokinesis). There is no weakness of the upper extremities and the gross motor power is apparently normal.

The supinator reflexes are present and not exaggerated. The

biceps- and triceps-jerks are not elicitable. The muscles are somewhat relaxed and free from any spastic phenomena.

On attempting to hold the outstretched arms and hands at rest there occur slight ataxic movements which are increased by closure of the eyes. Objects placed in either hand with the eyes closed are promptly recognized and the stereognostic sense is unimpaired. The direction of passive movements of the fingers, wrist and elbow are promptly recognized with the eyes closed. With the eyes closed an attempt to place the segments of the upper extremity on one side in the same position as the other cannot be accomplished, owing to the ataxia.

The gross motor power of the lower extremities is well preserved and there is no special atrophy of the musculature. Passive movements are quite free, the muscles are relaxed and there are no evidences of spasticity. There is, however, marked incoördination of movement in the recumbent posture. The attempt to place the heel upon the knee or to elevate the extremity in a straight line produces a marked irregularity and incoördination of movement, which is sometimes accompanied by slight atactiform jerking movements of the head, trunk or upper extremities. The knee-jerks are elicitable and about equal on the two sides. They are not exaggerated and the responses are rather subnormal. The Achilles-jerks are faint and not always elicitable. The plantar reflexes are of the normal type (no Babinski).

Lying perfectly quiet and in a relaxed posture no choreiform or athetoid movements are present. If the arms and legs are then simultaneously elevated and the attempt is made to hold them in this position a great disorder of coördination immediately results usually with loss of balance and a tendency to roll over. The abdominal and epigastric reflexes are present and active on both sides.

The motor cranial nerves are normal. There is no paresis of the ocular, facial or palatal musculature. On protrusion of the tongue there are slight atactiform movements of the head and trunk, and in a lesser degree on testing the facial innervation or on fixing an object with the eyes.

There is no nystagmus. The pupils are equal and react to light and accommodation. The corneal and conjunctival reflexes are active. The jaw-jerk is not elicitable. Articulation is thick and indistinct. This is an ataxic, dysarthric disturbance of speech, and to the untrained ear is very difficult to understand.

There is no forced laughter, but the act of laughing is accompanied by ataxic movements of the head and trunk and to some degree of the extremities. The acts of deglutition and mastication are also accompanied by slight ataxic disturbance.

The special senses are not affected. Vision, hearing, and the sense of smell are normal. The optic nerves are normal.

The general sensibility is apparently undisturbed. Taetile, pain and temperature sensations are normal, and their localization, so

far as could be determined, was fairly accurate. The posture sense of the upper and lower extremities was apparently preserved and upward and downward movements of the joints were promptly recognized.

Heart and lungs are normal. Urine negative.

Mentally the child was bright and responsive and carried out the various tests promptly and intelligently. She was able to spell and could read short sentences, and the mother stated that she was making steady progress. She was cleanly in all of her habits and has had good control of the sphincters since early childhood. There has been a marked improvement in the child's condition during the past few years, but she still required constant care and supervision because of the general motor disability.

*Resumé of the Clinical Reports.* The cases which have just been described are very similar in their etiology and general clinical characteristics and constitute, I believe, a well-defined clinical type of cerebral birth palsy. They represent an ataxic type of cerebral diplegia which stands in striking contrast to the spastic type of Little and the flaccid or atonic type of Förster.

In all of the cases there was a history of severe injury at birth followed by retarded and defective development of the power of motor coördination. There was no paralysis, and if such existed after birth it was of a transient nature and the gross motor power was eventually completely restored. There were no evidences of spasticity. The active and passive movements as well as the reflexes revealed none of the characteristic signs of pyramidal tract involvement. The tonus of the muscles was slightly reduced and the tendon reflexes showed a corresponding reaction, and were moderately diminished and difficult to elicit. There was no undue flexibility of the extremities as occurs in the severer forms of hypotonia.

The essential symptom was a generalized ataxic disturbance affecting the gait, station, articulation and the use of the individual members. This was present in all positions, including the recumbent posture, and I would particularly emphasize the persistence of an ataxic disturbance of the arms and legs in the recumbent posture when no effort was required to maintain the equilibrium. The ataxic disturbance was also increased by closure of the eyes, by mental excitement and by any effort to carry out precise and definite movements.

The disturbance of coördination was bilateral and fairly symmetrical, but one side may show a greater degree of involvement. It affected the finer movements of the hands and fingers as well as movements of the larger joints, and seemed to be equally distributed in this respect. There was, at times, a slight tendency to motor unrest, somewhat suggestive of a choreic disturbance, which I regard as a manifestation of ataxia and the effort to maintain posture. The disorder of motility was clearly ataxic, and was

characterized by an inability to carry out precise and definite coördinate movements. It was not in any sense a true chorea or athetosis, the restless atactiform movements in certain postures merely suggesting the choreiform tendency. Dysarthria was also a well-marked symptom, and was regarded as part of the ataxia. There was no nystagmus. The sensibility, both superficial and deep, so far as could be determined by the usual clinical tests, was quite normal. Especially noteworthy was the preservation of the sense of posture and the stereognostic sense. In none of the cases was there a serious mental defect. The retardation was no more than might follow a severe disturbance of speech and incoördination and the restriction of opportunity imposed upon the child.

In none of the cases was there any tendency to grand mal or petit mal seizures. The convulsions occurring immediately after the birth had manifested no tendency to recur in later life.

Some improvement had taken place in all of the patients, and there were no indications of an increasing mental deterioration or progression of other symptoms. In this respect the ataxic form resembles the spastic type of Little with its well-recognized tendency to improvement.

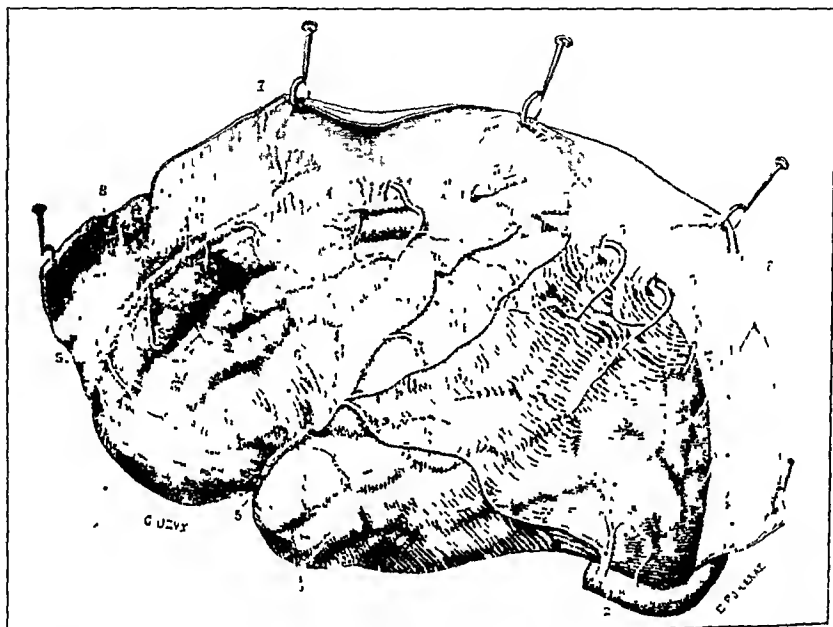
This very striking disturbance of motor incoördination I would refer to a disorder of the cortical functions, probably the result of a bilateral injury to the parietal area at birth. A lesion of this character would interfere with the development of the higher cortical centers engaged in the reception and elaboration of the memories of movements, and produce a *pure cortical ataxia*; or it might interrupt the commissural symptoms by which these memories are communicated to the motor area for the proper regulation of coördination, with a resulting *transcortical ataxia*. In either event a serious loss of the control and regulation of movement would of necessity result.

The primordial cortical centers which receive muscle and posture sensibility are not affected, for the general sensibility, both superficial and deep, is apparently preserved. It is probable therefore that the cortical centers subserving the function of common sensibility are either not included within the limits of the destructive lesion or, if they are injured, their function is subsequently restored by the compensatory activities of other centers, cortical and infracortical.

*Pathological Considerations.* The pathology of this group of cases in the absence of definite pathological evidence may only be surmised. I believe, however, that we are justified in the assumption that the lesions are of the same general character as have been found associated with other types of the cerebral birth palsies, differing only in their localization.

The pathological studies of Kundrat have shown that thrombosis of the superior longitudinal sinus with occlusion or rupture

of the cerebral veins is a by no means uncommon sequel of injury to the child's head during birth. This form of lesion is very probably favored, if not directly induced, by overlapping of the parietal bones during the process of molding of the fetal head. During the course of a prolonged and difficult labor, instrumental delivery, or precipitate parturition, the delicate cerebral veins may be torn from their connections as they traverse the intermeningeal space to enter the sinus, with consecutive hemorrhage over the surface of the brain, either subdural or intermeningeal.



Showing distribution of the cerebral veins on the external surface of the hemisphere. The dura mater is lifted to show the termination of the veins in the superior longitudinal sinus. 1, superior longitudinal sinus, 2, horizontal portion of lateral sinus; 3, large anastomotic vein of Trolard, 4, anastomotic vein of Labbé, 4', anastomosis between the vein of Trolard and the superior longitudinal sinus, 5, 5, 5, ascending veins of the hemisphere, 6, 6, 6, descending veins, 7, branch of the middle meningeal anastomosing at 7' with an ascending cerebral vein as it enters the sinus, 8, dura mater. (From Testut's Anatomy.)

The subdural type of hemorrhage is usually massive, consisting of a single large clot, and is commonly unilateral. Intermeningeal hemorrhages are more diffuse, often bilateral, and consist of a thin film-like clot of blood confined by the piaarachnoid. This is greatest in the region of the superior longitudinal fissure where the cerebral veins cross to the sinus and gradually tapers off as it passes over the surface of the hemisphere toward the fissure of Sylvius. As the larger veins run their course in relation to the fissures there is a natural tendency for the blood to follow and gravitate in the depths of the larger cerebral sulci. Limitation of

the vascular lesion to the region of the fissure of Rolando would explain the occurrence of spastic diplegia, and a similar explanation might be offered for the manifestations of cerebral diataxia, namely, thrombosis or hemorrhage limited to the parietal veins of the cerebral cortex (see figure).

Kundrat also emphasized the importance of structural peculiarities of the margins of the parietal bones and intervening membrane to injuries of the sinus. He expressed the belief that thrombosis and hemorrhages of venous origin are much more likely to occur in infants with firm bony edges and narrow interosseous membranes, because of the mechanical interference with overlap in the process of molding of the fetal head. A narrow interstitial membrane and parietal bones, with thick heavy margins, would render the sinus liable to the dangers of compression, with consecutive thrombosis or hemorrhage of the cortical veins. Kundrat also performed the interesting experiment of attempting an injection of the cerebral veins through the exposed sinus while holding the parietal bones firmly in a position of overlap, and found that the backward flow of blood through the sinus was effectively blocked by the compressive action of the bones. The dangers of such a contingency in long-protracted labor are obvious notwithstanding the rich collateral circulation of the cerebral venous system.

The essential lesions of the cerebral birth palsy consist therefore of hemorrhage either subdural or intermeningeal, with more or less thrombotic softening of the cerebral cortex from obstruction to the cerebral venous system. These may occur in various combinations. In grave cases lacerations of the brain substance, ventricular and intracerebral apoplexy and hemorrhages at the base of the brain are occasionally observed. Involvement of the cortical venous system is, however, the most important from the clinical point of view, as the severer forms of injury are usually rapidly fatal and therefore have little more than a pathological interest.

Studies of the cerebral cortex in cases of sinus thrombosis also show that intermeningeal hemorrhage is by no means the most important factor in producing the serious consequences of birth palsy, but that grave and permanent changes in the cortex itself may result. Thrombosis of the cerebral veins produces retrograde engorgement of blood, with punctate hemorrhages in the corresponding vascular distribution, and is associated with edema, perivascular engorgement and degeneration of the ganglion cells. (Hunt.) Although a certain degree of collateral circulation may be established, the delicate cells and neurons of the superficial layers of the cerebral cortex would inevitably suffer considerable damage.

Any limitation of the venous thrombosis to a definite vascular distribution would play a very important role in the causation of



special clinical types and would explain the occurrence of purely spastic or purely ataxic types of this affection.

In the majority of cases the effusion or thrombosis takes place in the motor areas, producing the spastic type described by Little. That this lesion may be quite circumscribed is shown by the not infrequent occurrence of purely spastic states without mental defect, epilepsy, chorea or athetosis.

The ataxic type of cerebral birth palsy is, I believe, the result of a more or less circumscribed lesion of similar nature within the confines of the parietal area behind the fissure of Rolando. The anatomical distribution of the parietal veins of the cerebral cortex render such a lesion not improbable, the effusion of blood and cortical degenerations interfering with the proper development of the various centers and commissural systems which subserve the higher functions of the coördination of movement (see figures). A lesion of this character might affect a dissociation of the sensory and motor spheres of the cortex, producing a condition in which motion would be possible and the sensibility preserved, and yet the harmony and coördination of movement would be lost, a form of *transcortical ataxia* in which there is an inability to convey to the motor area the complicated memories of movements and their combinations, so essential for a precise coördinate act.

That the parietal lobes contain important centers for muscle sensibility and the memories of movements has been shown by a number of observers and is accepted by all authorities on cerebral localization. The parietal sensory area includes the postcentral convolution, the superior parietal lobule (Pr) and the inferior parietal lobule (Pri) and portions of the supramarginal and angular gyri. It includes as well the precuneus on the mesial surface of the hemisphere.

In this region are stored not only the sensations of individual joints and muscles, the proprioceptive sensibility proper, but also the higher and more complicated motor memories, the various acquired psychic memories of movements which are essential for the development of a finer and more delicate system of coördination.

Von Monokow has suggested that the *fasciculus centroparietalis*, an association bundle uniting the angular gyrus and the Rolandic area, may play a role in the cortical association of muscle sensibility. He regards the parietal convolutions Pr and Pri and their association tracts as of special importance for the representation of movements and combinations of movements. The sensations of the individual muscle groups and segments and tactile sensibility he would localize in the postcentral convolution.

It is now generally held that the simple perception of deep sensibility, including the muscle sense and the sense of posture, are localized in the ascending parietal convolutions (postcentral gyrus), probably in segmental relation to the corresponding motor

centers of the central convolutions (Mills), while the higher psychic perceptions of motor activity, namely, the memories of movements and combinations of movements are situated more posteriorly in the superior and inferior parietal lobule, a region which is concerned with the registration of higher motor memories.

Indeed, it is quite conceivable that the centers which are engaged in the perception of deep sensibility might escape or recover from the effects of a lesion, and yet the higher centers and commissural systems which register and transmit the more complicated motor memories be seriously impaired.

The view which has just been expressed as to the pathology and localization of the lesions in cases of cerebral birth palsy receives a certain confirmation from the clinical and pathological investigations of Holmes and Sargent of injuries to the superior longitudinal sinus from gunshot wounds of the head. In their large series of cases, comprising seventy observations, the conspicuous feature of the clinical picture was a bilateral spastic paralysis, with marked rigidity involving the legs, trunk and arms in the order named. Articulation and the movements of the face were usually not affected. The paralysis was greatest in the legs and gradually diminished in an upward direction, thus corresponding to the arrangement of the motor centers in the Rolandic area. The accompanying muscular rigidity was extreme. By analogy one might say that such cases corresponded to the spastic type of Little's disease in which cortical hemorrhages and thrombosis of the longitudinal sinus and cerebral veins play an important role.

Sensory disturbances were also occasionally noted by Holmes and Sargent and their sensory investigations are of interest as bearing on the symptomatology of lesions of the parietal lobe. Their summary is as follows:

"The sensory disturbances are especially interesting, as they are almost always those of a pure cortical lesion unaccompanied by any shock effect. The appreciation of pain and temperature is unaffected, and there is no definite diminution of tactile sensibility, but a certain number of light contacts are not recognized; there is, however, no threshold alteration, and the proportion of those missed is not directly related to the intensity of the stimulus. On the other hand, the localization of tactile stimuli, the recognition of the position and of passive movements of the limbs, and of form, shape and size, as well as the discrimination of the compass points, may be seriously disturbed. The slowness of the affection of cutaneous sensibility has been frequently astonishing, as many patients have complained spontaneously of numbness and of having 'no feeling' in their legs." One of their cases was of special interest as indicating the possible course of events in the infantile ataxic group, the motor paralysis clearing up rapidly, with persistence of a high degree of ataxia.

It should be emphasized that these studies were made upon adults in whom cortical function was fully developed in contradistinction to the infantile group in which cortical centers and systems are still immature and in which several years must elapse before accurate sensory examinations are possible. This may in part explain the preservation of common sensation in the infantile group, with loss of the power of coördination.

In all other forms of ataxia, save the cerebellar ataxia, there is a disturbance of the deep sensibility, the degree of which usually determines the severity of the motor disorder. This is true of the peripheral, spinal, thalamic and cerebral ataxia.

Why should the deep sensibility be preserved and yet a severe degree of motor incoördination be present in the ataxic birth palsies? No definite answer can be given to this question at the present time which is not more or less theoretical in nature.

In the first place it is possible that the cortical representation for the perception of deep sensibility covers a larger field than is usually held—as is true according to von Monokow of the cortical motor zone, and thus a considerable area might escape injury. As the lesion occurs in early life there is also ample opportunity for compensatory replacements and substitutions on the part of subcortical centers and neighboring regions of the cerebral cortex. It is also possible that the sensory area for the perception of muscle sensibility is limited to the postcentral convolution and so might escape entirely the ravages of the lesion.

In the course of development of the cortical functions of motility the acquired memories of movements and their complex coördination are registered in a manner similar to the storing of the speech memories. These engrams represent a higher sensory elaboration of movement and would be all-important in the carrying out of precise and definite motor acts. If the region of the parietal cortex subserving this higher function of motility were injured on both sides in early life these memories would be improperly registered or the commissural fibers, through which they exert their influence on motility, would be interrupted with a resulting disharmony of movement. This would produce a cortical or transcortical ataxia, a disorder in the sphere of movement similar to apraxia or agnosia, in which the mechanism for the reception or transmission of higher motor memories would be seriously impaired, the bilaterality of the lesion preventing any compensatory activity on the part of the opposite hemisphere.

As the injury to the cortex takes place at birth, and as these cases cannot be subjected to accurate sensory tests much before the sixth or seventh year, there is ample opportunity for restoration and substitution of function. It is therefore not altogether surprising that the deep sensibility is preserved in conjunction with incoördination of the general motor activities. The cortical

centers subserving the function of protopathic sensibility either escape injury or are capable of being replaced by the compensatory activity of adjacent cortical areas.

The higher coördination activities of the muscular system are gradually acquired and are especially retarded and slow of development in this group of cases. That even these are susceptible of gradual development is shown by the clinical course of the cases.

*Clinical Comments.* The cerebral diatxia bears a certain resemblance to the cerebellar ataxia. The gait, like the cerebellar gait, may be somewhat titubating; there is dysdiadokokinesis and the speech has a dysarthric character not unlike that observed in cases of cerebellar disease. There is, however, no nystagmus, the disturbance of movement is not a dysmetria but a true ataxia, and the ataxia of the extremities is marked and persists in the recumbent posture. In the recumbent posture, with the extremities elevated and the eyes closed, there are ataxic movements, such as are observed in spinal ataxia and unlike the true cerebellar ataxia. Furthermore, the ataxia of the distal portion of the extremities is quite evident. There is also, especially during effort and mental excitement, a tendency to atactiform movements, of a more general character, which resemble or rather suggest a choreiform disturbance. They are not, however, spontaneous, but disappear in the relaxed and recumbent posture and appear only during muscular effort and movement. They are to be regarded as compensatory ataxic manifestations, similar to those occasionally observed in other forms of ataxia.

Another point of interest is the presence of a slight degree of hypotonia. It is well known that lesions of the parietal lobe may produce hypotonicity of the musculature, with diminution of the tendon reflexes. It is therefore not surprising to encounter a certain degree of hypotonicity in conjunction with cortical ataxia from lesions of the parietal lobe. In some of the cases described as cerebellar or atonic-astasic types of diplegia the nature of the ataxia and the associated hypotonia are somewhat suggestive of a parietal localization. This opens up a field for future investigation, and it is my belief that certain symptoms of diplegia which have heretofore been relegated to the cerebellum are really of cortical origin and referable to the higher cerebral centers for the control and coördination of movement.

In the above description I have attempted to outline the chief clinical features of the ataxic type of cerebral birth palsy or cerebral diatxia. It is the sensory equivalent of spastic diplegia, and like this affection shows a similar tendency toward improvement. In a pure form it is, however, comparatively rare.

Some of the cases probably recover or show a very considerable degree of improvement, and are then regarded as of cerebellar origin, an interpretation in which I was originally inclined to par-

ticipate. After a more detailed study of the motor phenomena, however, I feel convinced that the cortical mechanism is the essential structure involved.

**THE ATAXIC DIPLEGIA.** This point of view finds a further confirmation in the not infrequent combination of ataxia and spastic paralysis in many cases of cerebral birth palsy, cases in which there are symptoms of generalized spasticity but modified by the association of ataxic symptoms. This constitutes a very grave form of the cerebral birth palsy, examples of which may be found in nearly every institution for the care of chronic diseases. The condition of motor weakness and spasticity being accentuated by the loss of the power of coördination.

Two such cases, aged ten and eleven years respectively, with the typical history of injury at birth, are at the present time under observation in my wards at the Montefiore Home and Hospital. Both cases are confined to the wheel chair and are unable to stand or walk. There is a generalized spastic state which is complicated by a profound general ataxia, any attempt to carry out a precise movement evoking a wild disorder of incoördination. There is no true chorea or athetosis, although the nature of the ataxic disorder suggests a choreiform disturbance.

The atactiform movements do not, however, occur spontaneously, but only on attempts at movement. This I believe is an important factor in differentiating the true chorea and athetosis.

Both patients are fairly intelligent and attend the hospital school. There are no epileptic manifestations. The speech is dysarthric, spastic and very difficult to understand. The sensibility, both superficial and deep, is normal. As in the pure ataxic type there is no demonstrable disorder of the sense of posture or the sense of movement. The stereognostic sense is preserved and any common object placed in the hand is promptly recognized. In these cases I believe there is a combination of lesions which involves the motor sphere causing general rigidity and also the parietal area with a resulting disturbance of coördination. The clinical picture is one of generalized spasticity and ataxia in combination, namely, a *diataxic diplegia*.

Many such cases are, I believe, regarded as choreiform or athetoid types of diplegia, the extreme atactiform disorder of movement simulating very closely chorea. If there is marked spasticity an athetoid tendency is suggested.

In a previous communication I presented the pathological evidence, indicating the relationship of chorea and athetosis to the caudate nucleus and putamen of the corpus striatum, and there can be no question as to the paramount importance of the corpus striatum in the production of true chorea and athetosis. While the relationship of the cerebral cortex to chorea and athetosis is

accepted by all systematic writers, the exact localization of this function is still one of the unsolved problems of brain pathology. In all such investigations the existence of a cortical diataxia should be carefully considered and its very close resemblance to such disorders as chorea and athetosis.

CONCLUDING REMARKS. A variety of clinical types of the cerebral palsies of childhood are now recognized, and as such are firmly established in medical literature. Important among these may be mentioned the various forms of the spastic type of Little, the atonic or flaccid type of Förster, and those of cerebellar origin.

In this paper I have directed attention to the existence of a pure ataxic type which may be distinguished from other forms as *diataxia cerebrealis infantilis*.

The infantile cerebral diataxia is a special form of the cerebral birth palsy in which the symptomatology is characterized by a generalized disturbance of coördination without evidences of paralysis, spasticity, epilepsy or serious mental defect. The sensibility, both special and general, is apparently unaffected.

The clinical picture is believed to be dependent upon a bilateral vascular lesion in the parietal region, viz., hemorrhage and softening in the distribution of the parietal veins, resulting from an injury at birth.

The parietal area of the cerebral cortex is concerned with the reception and elaboration of higher motor memories, and a bilateral lesion in this region in early life would seriously interfere with the proper development of its cortical centers, association fibers and commissural systems. This would produce a disorder of the higher cortical functions of coördination—with a resulting *cortical* or *transcortical ataxia*.

The disturbance of coördination affects the speech, the gait and station and the use of the extremities, and is a pure ataxic disturbance.

It may be distinguished from cerebellar ataxia by the character of the motor disorder, its persistence in the recumbent posture and the absence of nystagmus. It may be regarded as the sensory equivalent of the spastic type of Little and is not infrequently encountered in combination with this affection, constituting a *diataxic diplegia*.

As in Little's disease, there is a tendency toward improvement, although the development of motility is always seriously retarded.

In its more severe forms this disorder of coördination may be associated with a tendency to atactiform movements which resemble superficially the phenomena of genuine chorea and athetosis; the recognition of which I believe to be of considerable importance in the eventual solution of the problem of the nature and localization of chorea and athetosis.

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ANGINA ABDOMINIS.<sup>1</sup>

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THE term *angina abdominis* was introduced by Baccelli to describe painful seizures in the abdomen due to aneurysmal for-

<sup>1</sup> Read before the American Gastro-enterological Association.

mations in the vessels of the celiac axis, or due to arteriosclerosis of these same vessels. Another name for the same condition has been offered by Huchard, *angina pectoris pseudogastralgique*. Inasmuch as the name invented by Baccelli has been accepted and used by recent writers, notably Pal, Brunton and Williams, Minella, Breitmann and others, it is the term which should be used in the future for this disease.

**CASE HISTORY.** The patient, a well-preserved woman, aged eighty-two years, apart from trivial illnesses of but short duration, has enjoyed good health for the greater part of her life. Twelve years ago she suffered with intense pain in the stomach, which was diagnosed at this time *carcinoma ventriculi*. In view of the present state of health the diagnosis is subject to question. Disregarding this attack, which resembled the seizure recently experienced, the patient rejoiced in the best of health and spirits until the early part of September, 1916. Following hard physical work connected with housecleaning, a task which no appeal to regard her years could make her depute to others, she was stricken with violent and intense pain in the umbilical region, which was accompanied by great anxiety, nervousness, restlessness and attempts at expulsion of gas per rectum and ex ore. These attacks having no relation to meals were repeated frequently, medication and diet proving unavailing, since September. She was seen by a surgeon in November, 1916, as gall-stones were suspected, but the diagnosis was not confirmed. Operation was disadvised, but no satisfactory conclusion was reached concerning the nature of the attacks. The surgeon's examination, which was most thorough, failed to reveal any organic lesion other than the arteriosclerosis.

The patient was counselled to remain in bed, to partake of nothing except milk, and was given a mixture of hydrochloric acid and pepsin, with occasional doses of sodium bicarbonate and nutmeg. For three days she was so much better that her physician permitted her to get out of bed, and again with utter disregard for her years, she cleaned a closet and laid unassisted a heavy carpet (November 23), being alone in the house at this time. Following this exertion she was seized with an excruciating pain in the umbilical region, with restlessness, extreme nervousness, attempts at expulsion of gas, no abdominal distention, no passage of urine or feces, some nausea, but no vomiting. The following morning this attack was duplicated in all characteristics except that the pain was less formidable. I saw the patient in company with the attending physician approximately about four hours after this second, and to date, last attack. The seizure on this day had been of short duration, as were all the others, that is to say, the acme of the frightful pain was sustained for only a few minutes, but intense abdominal soreness followed, and was present when I saw her, and lasted for a period of about twenty-four hours.



I found the patient (November 24) to be a remarkably well-preserved old lady, of frail build. The pulses were equal, regular, normal in rate, but the vessels were hard and easily palpable. The heart examination revealed a faint systolic murmur at the base, which was interpreted as being caused by aortic roughening.

The stomach was slightly dilated, there was a splash (milk had been ingested but a short time before) and some diastasis of the recti. The abdomen was very sensitive to pressure, particularly in the umbilical region, corresponding to a circular area about 6 inches in diameter, having the umbilicus as its center. There was marked throbbing of the abdominal aorta, no evidence of any enlargement of the vessels, and no murmurs. The reflexes were normal and the lower legs were slightly edematous. A rectal examination made by the surgeon five days previously, and being reported negative, was not repeated. The urine has contained albumin, but no sugar or casts. The blood-pressure was not taken at this time, as I had neglected to take my instrument, having been told it was essentially a stomach case. My neglect in this respect I have since regretted, as my request to the attending physician for a subsequent report of the blood-pressure was overlooked. However, four months later the pressure was found to be 130-60.

I believed we were confronted with an almost typical case of angina abdominis, and although skeptical as to the correctness of this view, the physician consented to give my therapeutic recommendations a trial. To the patient was explained what we believed to be the cause of her distressing attacks, and we gained her support in the view that physical overexertion or nervous strain, or both, were predisposing factors in calling an attack into being. Therefore the recommendation to rest during the day, and particularly a half-hour's rest on the right side, with a hot-water bottle to her abdomen following her meals, was readily agreed to. She was permitted to eat anything sparingly at the regular hours for meals and a glass of milk with a biscuit between meals. Only meat was restricted. Nitroglycerin, gr.  $\frac{1}{100}$ , was given every three hours, and potassium iodide, gr. x, three times a day. Pearls of amyl nitrite were left in the event of a recurrence of the pain.

Since November 24 the patient experienced the beginning of an attack, but the attack was cut short by the prompt use of amyl nitrite, and since that date there have been no further attacks. Potassium iodide and nitroglycerin have long since been discontinued; the patient is active in Red Cross work, and seems to be enjoying the best of health, the fear of cancer having, to her great relief, been permanently dispelled from her thoughts.

The symptoms as disclosed by the history of this patient seem almost typical of what has been described by others as angina abdominis, and a further discussion of the symptomatology of a classical case would seem unnecessary. Permit me to recall the

cardinal facts. The main feature of this woman's illness was the sudden agonizing pain which was directly associated with physical overexertion or nervous shock, thus in a way resembling the onset of angina pectoris. There is a prevalent notion that all attacks of angina pectoris are determined by emotional or physical effort, yet from Heberden himself we learn that attacks may occur during sleep and often during rest. Diderot records an attack which aroused him from sleep (Allbutt). Nevertheless, many cases of angina pectoris are precipitated by exertion, and in this patient of mine effort seems to have been the exciting factor. The pain is described by the patient as being horribly severe, and after the first seizure the dread of another and the realization that others were to occur, since the attacks were repeated, made her life one of continuous apprehension.

Accompanying the pain there were efforts at expulsion of gas by mouth and rectum, and when belching could be effected there seems to have been some slight relief. The bowels were slightly constipated. There was slight nausea but no vomiting.

The situation of the pain was about the umbilical region and radiated to the back, and following the seizure there was great sensitiveness on slight pressure about the umbilical region for an area 6 inches in diameter.

The diagnosis should not be difficult, and to my mind the main support of the correct diagnosis should be based on the frightfulness of the pain, the short duration of the same, the occurrence of the pain in arteriosclerotic individuals, usually advanced in years, in whom, apart from the arteriosclerosis, there can be found no appreciable sign of disease. Men are said to be more frequently affected than women.

The differential diagnosis must, in some cases, be made between abdominal angina and other diseases associated with gastric crises. Here it may be stated that Allbutt believes that epigastric angina is but a somewhat aberrant form of ordinary angina, and due, broadly speaking, to disease of some part of the thoracic aorta; but in angina "more definitely abdominal," he thinks it may be due to disease of the lower portion of the aorta or in other large vessels there. Osler is disposed to discredit the diagnosis, regarding abdominal angina as but the abdominal symptoms of angina pectoris. In this patient of mine, despite her years, no symptom of any cardiac disease had been complained of. There were no transient seizures without pain in which "there was a general suspension of the minor operations of nature for three or four seconds," called *angina sine dolore*.

Abdominal aneurysm should not be a matter of much moment in the differential diagnosis, as the pain is never anginoid, but rather boring in character, and situate in the left abdominal region. (Of 179 cases reported by Nixon none had anginoid pains.)

Tabes dorsalis should be readily distinguished, as the reflexes point the way to the true diagnosis, unless, unhappily, the patient is a sufferer from both tabes and from angina abdominis. The pain in tabes is intercostal rather than abdominal.

*Closure of the mesenteric vessels* I mention as an improbable differential diagnostic difficulty, on account of its extreme infrequency and because of the impossibility of recognizing the condition, unless one has been the observer of a previous case. Closure of the mesenteric vessels may take place in either the veins or arteries as a result of thrombosis or embolism. For thrombosis, arteriosclerosis itself is an underlying predisposing cause; for embolism valvulitis is the contributing factor. The onset of mesenteric closure is sudden and leads rapidly with great pain to collapse. Bloody vomitus is seen, and the stools, which contain blood, may be either obstipated or diarrheic. The abdomen becomes distended, painful and resistant to touch, with dulness in the dependent portions of the abdomen. The temperature is normal, pulse is rapid and soft and the patient gives the impression of one suffering with severe peritonitis or intestinal obstruction. In no case should abdominal angina be mistaken for mesenteric closure.

I should prefer to leave the question of pathology undiscussed, as but few cases have been studied satisfactorily from the clinical and pathological sides. Various suppositions have been suggested, but "clinical and pathological precision has yet to contribute to a better analysis of these phenomena." (Allbutt.)

So far as therapy is concerned, rest is an important measure, and avoidance of physical or nervous strain is to be recommended. Diet is to be that generally recommended for individuals of advanced years. Massage and faradization of the abdomen have been advised, and the homely hot-water bottle is not to be despised. Potassium iodide, sodium nitrite, sodiotheobromin, salicylate, nitroglycerin, amyl nitrite may each have its place, alone or in careful combination. During an attack if amyl nitrite fails, morphin, hypodermically, may be employed.

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## THE RELATION OF LUPUS ERYTHEMATOSUS DISCOIDES TO TUBERCULOUS INFECTION.

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THE etiology of lupus erythematosus has been one of the obscure problems of dermatology ever since the first description of the dis-

ease by Cazenave<sup>1</sup> in 1851. Investigations up to about the year 1910 have all tended to show that the disease is in some way related to tuberculosis. At first the belief seemed to be that it was a true inoculated tuberculosis of the skin. (Riel and Paltauf;<sup>2</sup> Klotz.<sup>3</sup>) Shortly after this, however, the tubercle bacillus toxin theory was elaborated and, led by certain French dermatologists (Hallopeau,<sup>4</sup> Boeck,<sup>5 6</sup> and Besnier), this theory seems to have been accepted by most observers as the probable etiological explanation.

In recent years doubt has been cast upon this theory. Unna,<sup>5</sup> Radcliffe Crocker,<sup>5</sup> Piek,<sup>7</sup> Sequeira and Balean,<sup>8</sup> Galloway,<sup>9</sup> Warde,<sup>10 11</sup> Pusey,<sup>12</sup> Engman and Mook<sup>13</sup> are all on record against it, although many of them and other observers believe that it is of toxic origin and should be classed with the polymorphic erythema group of skin diseases.

The basis for the tubercle toxin theory was the frequent finding of evidence of tuberculosis both clinically and postmortem. It is unnecessary here to go into the literature and review these statistics. Suffice it to say that in a large proportion of cases of this disease it has been observed that (a) there is a family history of tuberculosis; (b) there has been a positive reaction to the tuberculin test; (c) that there is clinical evidence of tuberculosis; (d) that evidence of tuberculosis was found postmortem. We shall take up these points and discuss them later.

We have studied 12 cases of lupus erythematosus discoides from the skin and tuberculosis clinics of the Washington University Dispensary. These cases were approached from as many angles as possible; a detailed history, with special reference to past and present illness and previous exposure; a careful physical examination together with roentgen plates; tuberculin tests; Wassermann reaction; and the pulse, temperature, and weight record. A brief synopsis of each case follows:

CASE I.—A. H., white; female; aged fifty years. C 1. No. 27846.

*Family History.* Negative.

*Personal History.* Erysipelas in 1889. Since then has never had any serious illness.

*Wassermann Reaction.* Negative.

*Tuberculin Test.* Positive; reacts to  $\frac{1}{2}$  ingm. O. T. but not to  $\frac{1}{10}$ .

Skin disease began at the age of forty-five years. Presents lupus erythematosus of the lips.

*Physical Examination of the Chest.* No evidence of tuberculosis found. Roentgen-ray plate; air content good, somewhat better in the lower right lobe than elsewhere. Right lung: arborization is distinct from rather dense hilus, with several small dense glands. Diaphragm normal. Left lung: similar to right.

*Diagnosis.* Healed tuberculosis of childhood. (Diagnosis made on roentgen plate.)

CASE II.—K. A., white; female; aged thirty-one years. C 1. No. 27842.

*Family History.* Negative.

*Personal History.* Never had any serious illness.

*Wassermann Reaction.* Not done.

*Tuberculin Test.* Positive; marked local reaction to  $\frac{1}{10}$  mgm. O. T.

Skin disease begun at the age of thirty years. Presents single patch of lupus erythematosus on side of nose.

*Physical Examination.* Harsh breathing, anteriorly and posteriorly in both lungs, but no increase in whisper; probably "cold."

*Roentgen Plate.* Fairly good air content in both lungs. Right lung: upper lobe shows thickening of interlobular lines, but no marked approximation. The hilus is fairly dense, but no definite nodules are seen. Extension to the lower lobe dense at the proximal area, but not in the axillary area. Diaphragm held at an angle of 90 degrees. Left lung shows thickening of the interlobular lines; no definite shadow. Hilus is fairly dense. Lower lobe markings faint, with diaphragm flattened. Diagnosis: Chronic tuberculosis; chronic pleurisy. No clinical tuberculosis.

*Diagnosis.* By roentgen rays shows evidence of an old chronic tuberculosis.

CASE III.—L. R., white; female; aged thirty-three years. C 1. No. 22585.

*Family History.* Grandmother and one cousin died of tuberculosis; otherwise negative.

*Personal History.* Measles, scarlet fever, mumps, pertussis, and varicella in childhood. Was very delicate as an infant. Following scarlet fever and measles, at the age of five years, was very "nervous" for a number of years. Malaria (?) at fifteen. Nervous prostration from sixteen to twenty. Smallpox at twenty-one. Typhoid at twenty-five, of moderate severity, followed by nervousness. Mild attacks of grip, bronchitis, and tonsillitis since then.

*Wassermann Reaction.* Negative.

*Tuberculin Test.* Von Pirquet positive in 1914. 1916 reacted to  $\frac{1}{10}$  mgm. O. T. and focal reaction in lesions.

Skin disease began at the age of twenty-nine years. Presents lupus erythematosus of face. Scars of old lesions on scalp, backs of fingers, and arms.

*Physical Examination.* Deficient fat. Slight muscle spasm in upper thorax on both sides. Breathing in left apex distinctly harsher than in right. Breathing in right apex seems to be diminished, but owing to the patient being nervous she does not breathe deeply. Whisper is normal. Slightly impaired resonance posteriorly. Roentgen plate. Fair air content in both upper lobes. Left lung: interlobular markings not approximated. Hilus not dense. Extension from hilus is dense, but not closely approxi-

mated. Right lung is similar to left except that the diaphragm is more regular.

*Diagnosis.* Early pulmonary tuberculosis. (Diagnosis made on history and physical examination. Roentgen plate shows nothing definite.)

CASE IV.—F. P., colored; female; aged thirty-six years. C 1. No. 32335.

*Family History.* One sister died of pulmonary tuberculosis; otherwise negative.

*Personal History.* Patient states that she had "serofula" in childhood, but can give no details. Has had no serious illness since.

*Wassermann Reaction.* Not done.

*Tuberculin Test.* Not done.

Disease began at the age of thirty-five years. Presents lupus erythematosus generally distributed over the face and under and on the ears.

*Physical Examination.* Impaired resonance over the right lung anteriorly, together with increased whisper both anteriorly and posteriorly. Diminished breathing on the right side posteriorly. No history of loss of weight, fever, or sputum.

*Roentgen Plate.* Not obtained (patient only made two visits to clinic). Diagnosis without roentgen rays is suspected tuberculosis.

CASE V.—E. F., white; female; aged forty-three years. C 1. No. 861.

*Family History.* Negative.

*Personal History.* Has no bearing on the case.

*Wassermann Reaction.* Negative.

*Tuberculin Test.* Positive; von Pirquet.

Disease began at about the age of twenty-six years. Presents lupus erythematosus. An extremely severe case of many years' duration, involving the face, ears, and neck in erythematous and scaly plaques, with much scarring and atrophy. Chilblain circulation.

*Physical Examination.* Expansion poor. No marked dullness, but some diminished resonance posteriorly. Diminished breathing in both lungs, both anteriorly and posteriorly. Whisper slightly increased, lower right anteriorly and upper left posteriorly. (Obesity of patient may account for diminished breathing.)

*Roentgen Plate.* Air content fairly good in both lungs. Left upper lobe between second and fourth ribs somewhat hazy. Hilus rather dense. Diaphragm normal. Right lung: hilus much denser than left. Several nodules seen. Some approximation of interlobular lines, especially of middle and lower lobes. Plate not taken in deep inspiration.

*Diagnosis.* Healed tuberculosis of childhood. No definite adult tuberculosis. (Patient received tuberculin treatment up to 20 mgm., with no effect upon the progress of the disease, but a focal reaction in the skin lesions was observed.)

CASE VI.—E. B., white; female; aged thirty-three years. C1. No. 15223.

*Family History.* Negative.

*Personal History.* Never had any serious illness.

*Wassermann Reaction.* Not done.

*Tuberculin Test.* Positive.

Disease began at the age of thirty years. Presents lupus erythematosus. Several small erythematous and scaly plaques on the sides of the nose and adjoining cheeks.

*Physical Examination.* No infiltration demonstrable by percussion. Slight muscle spasm anteriorly and posteriorly of right thorax. Whisper sound increased posteriorly in right upper lobe. Few moist rales in left lung anteriorly and an occasional rale in right lung posteriorly. Roentgen plate. Air content in both lungs fair. There is an approximation of the interlobular lines in both upper lobes, but no thickening. The hilus on both sides is dense. The costal angles are deep. Plate not taken in deep inspiration. Temperature showed an occasional rise to 99+, and with the physical examination make diagnosis of pulmonary tuberculosis.

CASE VII.—F. S., white; male; aged thirty-four years. C1. No. 18058.

*Family History.* Negative.

*Personal History.* Never had any serious illness.

*Wassermann Reaction.* Not done.

*Tuberculin Test.* Not done.

Disease began at about the age of twenty-five years. Lupus erythematosus. Scaly, erythematous plaques on nose and cheeks.

*Physical Examination.* Breath sounds are distant and diminished in both upper lobes. Whisper is increased in the right lung, more marked in the upper lobe posteriorly. Muscle spasm in posterior right thorax. Expiration prolonged and harsh posteriorly.

*Roentgen Plate.* Shows good air-containing lungs. The hilus on both sides is dense, with fairly dense extension. Both apices clear. Interlobular markings are distinct and not dense. Diaphragm normal.

*Diagnosis.* Chronic hilus tuberculosis (?). (Diagnosis made by roentgen plate and physical examination.)

CASE VIII.—L. K., white; female; aged forty years. C1. No. 32106.

*Family History.* Negative.

*Personal History.* Never seriously sick.

*Wassermann Reaction.* Negative.

Disease began at the age of thirty-nine years. Lupus erythematosus. Small erythematous, scaly patch on side of nose.

*Physical Examination.* Harsh breathing over the bases of both lungs posteriorly, with slight increase of whisper. No definite signs of tuberculosis.

*Roentgen Plate.* Air content of both lungs good. Right lung: bronchial branches well marked and can be traced to periphery. Hilus very dense, with extension to lower lobes slightly thickened. Several large dense glands are seen. Diaphragm negative. Costophrenic angle deep. Left lung: apex slightly hazy as compared to right. Otherwise findings are similar.

*Diagnosis.* Healed tuberculosis of childhood. No adult tuberculosis.

CASE IX.—E. B., white; female; aged forty-five years. C 1. No. 28632.

*Family History.* Negative.

*Personal History.* No bearing on case.

*Wassermann Reaction.* Negative.

*Tuberculin Test.* Not done.

*Sputum Examination.* Negative for tubercle bacilli.

Skin disease began at the age of forty-four years. Lupus erythematosus. Plaques scattered over the front and side of the face.

*Physical Examination.* Breath sounds diminished in both upper lobes. Few shifting, dry, and moist rales in both upper lobes. Impaired resonance in both upper lobes, anteriorly and posteriorly; not marked, however. Lower lobes normal.

*Roentgen Plate.* Air content fair, less in upper lobes. Right lung: Upper lobe, arborization thickened and interlobular lines are more or less approximated in axillary and mammary lines. Hilus dense, with many dense nodules. The extension to lower lobe is thickened and somewhat interlaced, with small pinhead-size points of density. Diaphragm normal. Costal angle deep. Left lung: Rather dense shadow in the upper lobe and marked thickening of the interlobular lines. A large nodule, size of a dime, is seen. Air content good in the lower lobes. Diaphragm irregular.

*Roentgen Plate.* Together with the physical examination and a constant temperature of 99° to 100° make the diagnosis of chronic pulmonary tuberculosis. Active tuberculosis of both upper lobes.

CASE X.—C. J., white; female; aged twenty-seven years. C 1. No. 21814.

*Family History.* One uncle by marriage died of pulmonary tuberculosis. Otherwise negative.

*Personal History.* Typhoid at twelve years. Frequent attacks of tonsillitis in childhood. Pus tubes and operation at age of nineteen, followed by "stomach trouble," which lasted on and off about six years. No history of syphilis.

*Wassermann Reaction.* Positive 4+.

*Tuberculin Test.* Not done.

Disease began at the age of twenty-four years. Presents lupus erythematosus. Extensive butterfly distribution.

*Physical Examination.* Right lung: anteriorly, breath sounds somewhat diminished except for an area in the second intercostal



space, near the sternum, where the breath sounds are very harsh and there is increased whisper. Lower lobe normal. Left lung: Upper lobe, anteriorly, breathing is diminished, but the whisper is loud here and there. Lower lobe is normal. Posteriorly, right lung, impaired resonance, with diminished breathing, no increased whisper. Left lung: breath sounds somewhat harsh, with increased whisper and impaired resonance. Lower lobes negative.

*Roentgen Plate.* Air content good in lower lobes, only fair in upper lobes. Left lung: Upper lobe: approximation of interlobular lines but not very dense. Many small dense nodules in this area. Hilus is broad and dense with several dense nodules. Lower lobe: bronchial arborization is not dense or interlaced. Diaphragm somewhat irregular. Lung dips deeply into costophrenic angle. Right lung, upper lobe, interlobular markings are dense but not as closely approximated as the left. Many nodules seen in this area. Hilus very dense and broad; many nodules seen. Middle lobe: arborization is distinct to periphery and there is a moderate amount of approximation. Lower lobe: arborization is dense and interlaced, and there is more or less approximation of interlobular lines. The proximal third of the diaphragm is held up by adhesions. Lung dips deeply into costophrenic angle.

*Diagnosis.* Chronic pulmonary tuberculosis. (Note: As the physical signs are not classical for tuberculosis and the Wassermann reaction is 4+ there is some doubt as to whether the lung condition is tuberculous or luetic.)

CASE XI.—S. W., white; female; aged thirty-one years. C1. No. 19292.

*Family History.* One aunt and two uncles died of pulmonary tuberculosis. Otherwise negative.

*Personal History.* Usual diseases of childhood. Generally good health until the age of twenty-four years, then had an attack of "inflammatory rheumatism," affecting the finger-joints only. At the same time had phlebitis in the right leg. The rheumatism in the fingers would get better and worse, and lasted about three years. The phlebitis kept the patient in bed about ten weeks and then got entirely well. About one year after this, phlebitis started in the left leg and kept the patient in bed about six weeks. Three weeks later the patient had a second attack of diphtheria. At the age of twenty-eight years she had two ulcers, one on each ankle, which eventually healed. No other serious illness. No menstrual disturbance.

*Wassermann Reaction.* Negative.

*Tuberculin Test.* Positive. Reacted to  $\frac{5}{10}$  mgm. O. T.

Skin disease began at the age of twenty-nine years. Presents lupus erythematosus. Plaques all over the face and ears.

*Physical Examination.* No definite signs of tuberculosis.

*Roentgen Plate.* Considerable air content. Left more than right. Right lung: there is no approximation of the interlobular lines of the upper lobes; a few small dense nodules are seen. The hilus is fairly dense and shows numerous nodules varying in size from a pinhead to a pea. Lower lobe: a few nodules are seen. The diaphragm is normal. Costal angle is deep. Left lung: interlobular markings are not distinct; no approximation. The hilus is less dense than the right. Lower lobe: the interlobular markings are distinct almost to periphery. Diaphragm is normal. The costal angle deep.

*Diagnosis.* Healed pulmonary tuberculosis of childhood. (No clinical tuberculousis.)

CASE XII.—N. D., white; female; aged fifty-two years. C 1. No. 18374.

*Family History.* As the patient remembers it one or two cousins had tuberculousis. Otherwise negative.

*Personal History.* Smallpox at eighteen months. Measles at five. Remittent (?) fever at fifteen. Both legs severely frozen at eighteen. Chronic rheumatism at thirty-seven; affected the knees and ankles and lasted one year. Ever since then gets slight attacks on occasion. Had a fatty tumor removed from the neck at the age of twenty-five. No history of lues. Never has been pregnant. Separated from husband for past twenty years.

*Wassermann Reaction.* Not done.

*Tuberculin Test.* Negative.

Skin disease began at the age of thirty-two. Present lupus erythematosus, butterfly distribution on face and a few lesions on scalp.

*Physical Examination.* Breath sounds in the right lung anteriorly are rather harsh, with no increased whisper. Left lung: upper lobe, breathing diminished, whisper not increased. Lower lobe: same findings. Posteriorly, similar findings. Chest is hyperresonant throughout.

*Roentgen Plate.* Shows a rather "brilliant" condition of both lungs, with the left extending farther down than the right. Left lung: hilus fairly dense, with several dense nodules. The interlobular markings are distinct to periphery, but are not approximated. There is a hazy appearance in the upper lobe near the axillary line. Diaphragm forms an angle of 90 degrees, the lung dipping down into the costal angle. Right lung: apex is cloudy. No interlobular lines seen. Hilus is quite dense, with numerous nodules. The interlobular markings are distinct to periphery, but not approximated. The diaphragm makes an angle of 90 degrees and is lower than the left. Lung dips deeply into the costal angle.

*Diagnosis.* Healed tuberculosis of childhood. Clinical diagnosis: chronic bronchitis; emphysema; chronic pleurisy (fibrinous).

We are therefore able to present 12 cases of lupus erythematosus

of the discoid type, 10 of which showed evidence of tuberculosis; 4 chronic tuberculosis; 1 active tuberculosis, and 5 healed tuberculosis of childhood. (We believe that the other 2 cases are tuberculous, but cannot present good proof.)

Let us compare these results with the results of others.

Boeck<sup>6</sup> investigated 36 cases and found pronounced symptoms of tuberculosis in 83 per cent. of them and a family history of tuberculosis in one-half of the balance of the cases. At a meeting of the Section on Dermatology of the British Medical Association<sup>5</sup> he gives the following figures: of 42 common, discoid, adult cases 28 presented indubitable evidence of tuberculosis, past or present, and 8 presented strumous ophthalmia: that is, 86 per cent. showed evidence of tuberculosis in some form.

Roth<sup>14</sup> collected 250 cases from the literature, and in 70 per cent. there was evidence, more or less pronounced, of tuberculosis.

Pick<sup>7</sup> reports that 18 of 43 cases of the discoid type showed evidence of tuberculosis (42 per cent.).

Sequeira and Balean<sup>8</sup> state that they found evidence of tuberculosis in 18 per cent. of their discoid cases and a family history of tuberculosis is not less than 80 per cent.

Kopp<sup>15</sup> found evidence of tuberculosis in 18 out of 38 cases (45 per cent.).

Gunsett<sup>6</sup> did 20 autopsies on cases of lupus erythematosus, and in only 9 was there evidence of tuberculosis.

A table was prepared for us of all the cases of lupus erythematosus of the discoid type appearing in the *British Journal of Dermatology* and in the *Journal of Cutaneous Diseases*. These cases numbered 225 in all. Tuberculosis was mentioned as being present or absent in only 64 of them. Of these 64 cases, 18, or 28 per cent., showed evidence of tuberculosis and 46, or 72 per cent., did not. In 69 cases mention was made of family history of tuberculosis; 28, or 40 per cent., were positive and 41, or 60 per cent., were negative. The tuberculin test was mentioned in only 9 cases, and of these 7 were positive and 2 negative. (These statistics were prepared by W. Kenneth Brown, of the senior class, Washington University Medical School.)

The statistics presented by Boeck and others led them to the belief that there was a direct connection or relation between lupus erythematosus and tuberculosis. Our statistics tally with many of theirs and, following out their line of thought, we might present the same conclusions; but our deductions, based on the modern conception of tuberculosis, are decidedly different.

We shall now take up in detail the evidence presented in the past, comparing it with ours and discussing its value.

First, all the evidence that has been presented is purely presumptive. We have been unable to find records of any work that shows a direct connection between the two conditions.

**FAMILY HISTORY OF TUBERCULOSIS.** Because quite a large percentage of cases of lupus erythematosus have a family history of tuberculosis it is presumed that this fact lends weight to the theory that there is a connection between the two diseases. Sequeira and Balean (*loc. cit.*) state that there is a family history of tuberculosis is not less than 80 per cent. of their cases. This is very high, and certainly might lend weight to the presumption were it not for other facts that must be taken into consideration. Boeck<sup>6</sup> finds a family history in only 8.8 per cent. of his cases. In our series 41.7 per cent. had a family history of tuberculosis. If we average these perhaps we shall come somewhere near the truth with 43.5 per cent. We are of the opinion that with careful questioning of patients fully as large a percentage could be found in many other conditions, say aene for instance. Then we would have to suspect that there was a relation between aene and tuberculosis.

**TUBERCULIN TEST.** "It is always found that between 40 and 60 per cent. of humanity react to the subcutaneous tuberculin test, provided that it be repeated with ascending doses three or four times" (Fishberg<sup>17</sup>). A positive tuberculin test indicates tuberculous infection and not necessarily tuberculous disease in a clinical sense (Hamman and Wolman<sup>18</sup>). Tuberculin has no effect on uninfected individuals (Hamburger<sup>19</sup>), but practically there are no uninfected individuals. We believe that Fishberg's statement can be modified to this effect, that practically all individuals above the age of twenty and living in large cities react to the tuberculin test. One of us (Singer) has been trying out the intradermic tuberculin test. In 49 out of 50 cases this test was positive; and here again we emphasize that the positive tuberculin test means tuberculous infection and not necessarily tuberculous disease. Our statistics, combined with those cases gathered from the *British Journal of Dermatology* and the *Journal of Cutaneous Diseases*, give 81 per cent. positive (13 out of 16 cases). With the intradermic test we have reason to believe that they all would be positive. A positive tuberculin test in cases of lupus erythematosus lends practically no weight to the theory that there is a relation between the disease and tuberculosis.

In this connection it would be well to discuss these facts; a focal reaction has occasionally been reported in the lesions of lupus erythematosus following the injection of tuberculin, and it is on record that lupus erythematosus has improved or been cured by the tuberculin treatment. The recent work of Engman and McGarry,<sup>20</sup> who caused the disappearance of the disease by the intravenous injection of foreign protein (typhoid and colon vaccine), shows that this is a foreign protein reaction and should not be interpreted as evidence of the relationship of the two diseases. Several of the cases which they report are included in our series, and we mention in particular their Case No. II, which is our Case No. V.

Here a focal reaction was observed in the lesions upon the injection of tuberculin. This case, as well as their other cases, cleared up wonderfully upon the intravenous injection of typhoid vaccine, *i. e.*, foreign protein. However, should we later on have to revise our conception of foreign protein reaction, these cases would still be open to question. They may easily have been lupus erythematoide of the Leloir type or lupus erythemato-tuberculeux of Besnier or a mixed type of lupus vulgaris and lupus erythematosus (Kyrle<sup>21</sup> and Spitzer<sup>22</sup>).

**CLINICAL EVIDENCE OF TUBERCULOSIS.** With modern methods of diagnosis, clinical evidence of tuberculosis can be discovered in an extremely large number of individuals. We venture to say, with little fear of contradiction, that fully 90 per cent. of all individuals above the age of twenty and living in cities are subjects of tuberculous infection or tuberculous disease. Tuberculous infection in early life is the rule and not the exception, and so by far the great majority of us are "vaccinated in childhood against tuberculosis." (E. L. Opie.) In our series of cases 83 per cent. showed evidence of tuberculosis, and we have reason to believe that this figure should be 100 per cent. But of the 10 cases showing indisputable evidence of tuberculosis, 5 showed healed tuberculosis of childhood, and certainly are not tuberculous in the sense that they were suffering from consumption; 4 cases showed chronic tuberculosis and also were not tuberculous in the sense that they were suffering from consumption. Only 1 case presented active tuberculosis. Healed tuberculosis of childhood means calcified nodules in the lungs or mediastina. Chronic tuberculosis means a walled off, fibroid condition. Therefore we make the point that in 9 out of 10 of our cases it is very improbable that a circulating tubercle bacillus toxin is responsible for the skin condition.

**POSTMORTEM EVIDENCE OF TUBERCULOSIS.** Kopp (*loc. cit.*) found evidence of tuberculosis postmortem in 18 out of 38 cases of lupus erythematosus. He does not regard his results as evidence of the tuberculous origin of the disease. We arrive at the same conclusion but by different reasoning.

From the time of Laennec (1831) up to the present more and more evidence of the ubiquity of tuberculous infection, as demonstrated postmortem, has been accumulating. Practically every succeeding investigator has found a higher and higher percentage of tuberculous infection and disease on his postmortem table. We shall refer only to the latest of these reports. (For complete discussion of this subject see Fishberg, *loc. cit.*, p. 33 *et seq.*)

E. L. Opie,<sup>23</sup> by a most ingenious method of postmortem investigation (roentgen-ray pictures of the inflated and extirpated lung followed by minute section and search with the skiagram as a guide), has had the following results: Of 50 patients dying of diseases other than tuberculosis, each and every one showed lesions of tuber-

culous infection or tuberculous disease. These cases were from all the services of the Barnes Hospital, and they furnish convincing proof of the ubiquity of tuberculous infection and tuberculous disease. The finding of tuberculosis postmortem, in our opinion, is not valid evidence of a relation between lupus erythematosus and tuberculosis.

The facts then are these: Fully 90 per cent. of adult humanity living in large industrial centers are the subjects of tuberculous infection or tuberculous disease. Moreover, practically no cases of lupus erythematosus are observed among the inmates of large tuberculosis sanitariums, and the histopathology of lupus erythematosus bears no resemblance to any known form of tuberculosis. We therefore maintain that there is no evidence of an etiological relation between lupus erythematosus discoides and tuberculosis. The rarity of the one and the ubiquity of the other, to say the least, argue strongly against any such relationship.

**SUMMARY.** Twelve cases of lupus erythematosus discoides were carefully examined for tuberculosis. All available diagnostic methods were employed and a conclusion was reached in each case by study of the combined results and not from any single diagnostic procedure.

Ten out of twelve of these cases showed indubitable evidence of tuberculosis, past or present, and it is believed that the other two are also tuberculous.

In only one of our series of cases that were definitely tuberculous was there any likelihood of the presence of a circulating tubercle bacillus toxin.

The evidence presented in the past to prove that lupus erythematosus discoides bears a relation to tuberculosis is purely presumptive.

Critical analysis of this evidence shows that conclusions drawn from it are based upon erroneous deductions.

**CONCLUSION.** In our opinion no evidence has been presented as yet that shows a relation between lupus erythematosus discoides and tuberculous infection or tuberculous disease.

It has been shown that tuberculosis past or present may be demonstrated in practically all cases of lupus erythematosus discoides, and this fact should only be interpreted as further evidence of the ubiquity of tuberculous infection and not as evidence of an etiological relationship between the two diseases.

We desire to thank Drs. George Dock and M. F. Engman for permission to use the cases reported and for their helpful suggestions in preparing this study.

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## ANEURYSM OF THE ABDOMINAL AORTA WITH RUPTURE INTO THE DUODENUM.

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THAT abdominal aneurysm is an infrequent condition both clinically and at autopsy is well known. Among 16,000 admissions to his wards at Johns Hopkins, Osler found only 16 cases; in Vienna 3 cases were found in 19,300 autopsies; Bryant has described 54 cases in 18,678 autopsies at Guy's Hospital; 13 cases in 6974 autopsies were found in the postmortem records of the Bristol Royal Infirmary.

Nixon, in 1911, collected and tabulated 233 cases of abdominal aneurysm including the above. Death resulted from rupture in 152 of these cases. In 149 the rupture took place either retroperitoneally or intraperitoneally; in 3 cases the rupture occurred into the gastro-intestinal tract; one of these, an aneurysm of the splenic artery, burst into the colon; the second is recorded as resulting in death from sudden collapse and profuse rectal hemorrhage. At autopsy cirrhosis of the liver was found, no mention being made as to the condition of the aneurysm, so that it is ques-

tionable whether rupture of the aneurysm or of a varix was the cause of death. The third case, a saccular aneurysm along the celiac axis and small aneurysm of the thoracic aorta, ruptured into the first part of the duodenum.

Since the publication of Nixon's tabulated series in 1911 there have occurred in the literature 11 other cases. Two of these cases ruptured into the gastro-intestinal tract. One case, reported by S. M. Zypkin, ruptured through a perforating ulcer into the stomach, so that at autopsy this organ was found filled with blood clot. The second case reported by E. A. Tozer ruptured into the duodenum. It was a saccular aneurysm of the abdominal aorta situated below the origin of the superior mesenteric artery. Tuberculosis of the aorta was found to be extensive and the etiological factor. Thus from a total of 244 cases 5 cases of abdominal aneurysm have occurred, with rupture into the gastro-intestinal tract.

The following are two cases, remarkably similar, of abdominal aneurysm which ruptured into the duodenum.

CASE I.—L. M., male, aged thirty-nine years, entered the Peter Bent Brigham Hospital June 25, 1916, complaining of "ulcer of the stomach."

*Family History.* Negative. Married sixteen years. Wife and two children well. One miscarriage. Habits are good; occupation hygienic.

*Past History.* Measles in childhood. Rheumatic fever fifteen years ago. He has had night-sweats for the past few weeks. There has been a loss of 20 pounds in weight in the last five months the patient thinks.

*Present Illness.* Started about January, 1916, with an indefinite sense of weakness. At that time the patient was worried over business affairs. There were "vague" symptoms which he could "not lay his fingers on." These persisted, and he thinks he gradually lost weight and strength. Previous to May 31, 1916, there is no history whatever of abnormal gastric or abdominal symptoms. On that day, while boarding a street car, he was taken with cramp-like pains "in the stomach." He walked into the car, sat down, fainted, and was unconscious for "ten minutes." When he came to he was covered with a drenching sweat. He proceeded home, arriving about one and a quarter hours later, and about ten minutes thereafter vomited fresh blood three times. The patient thinks that he vomited a considerable quantity, but has no idea as to the amount. He has since been on a restricted diet, and has been in bed practically all the time. There have been five subsequent spells of vomiting fresh blood, the last occurring eleven days ago. The patient has grown progressively weaker and more exhausted. His wife has noticed that most of the stools in the past four weeks have been tarry.



*Physical Examination.* The patient was a man, aged thirty-nine years, of medium stature, emaciated. On admission his gait was staggering, evidently due to weakness. Examination of his head, neck, lungs, heart, extremities, and reflexes was unimportant. His pulse was good. There was no thickening of any of his peripheral arteries. His heart was somewhat irregular. Examination of his abdomen showed distinct pulsations in his epigastrium. In the region of the pulsations there was felt a firm, smooth, non-tender mass in close apposition to the aorta, moving with each pulsation. No expansile pulsation could be made out in this mass, which measures 7 cm. x 5 cm. It did not move with respiration. Gurgling sounds were heard over the stomach area and the region of the mass, which was at about the anatomical location of the pylorus of the stomach.

*Examination of urine* was negative. On admission his hemoglobin was 25 per cent.; red blood cells, 1,392,000; white blood cells, 5200, with marked variation in size and shape and occasional polychromatophilia.

*Wassermann* on blood was negative.

*Gastric analysis* showed a positive guaiac reaction and microscopic blood.

*Stool* was black, formed, tarry. Guaiac positive.

*Roentgen Examination.* Unimportant.

*Course.* On the day of admission the patient ran a slight fever, the temperature ranging from 99° to 100°, but thereafter showed a daily range from 97° or slightly above to 99° or slightly above and the pulse rate for the most part varied between 70 and 80, and the respiratory rate between 20 and 25, until the day before exodus. The stools continued to show occult blood. On July 1 the patient vomited black blood clots, about 4 liters in all. Earlier that morning he had passed stools, consisting of black cast-like clots showing peristaltic impressions. His hemoglobin fell somewhat but his red blood cells remained unchanged. He became blanched and weak, dying within a few hours of respiratory failure.

Autopsy was performed eleven and a quarter hours postmortem. The body was that of a man, aged thirty-nine years, well developed, emaciated. The heart showed a chronic adhesive pericarditis, a moderate degree of fibrous myocarditis. The left coronary artery appeared normal. Just distal to its origin in the right coronary there was found a small, red, irregular, elevated mass about 0.5 cm. in diameter, composed of a friable laminated tissue, on the surface of which fresh fibrin was deposited. Its lumen was dilated at this point. Histological examination showed the intima to be thickened and hyaline, the surface of the intima ulcerated and covered with fresh fibrin.

The lungs, liver, spleen, and pancreas showed no lesions of importance. There was some edema of the kidney. A moderate

degree of arteriosclerosis was found diffusely distributed throughout all these organs. There was a marked secondary anemia.

The lesions in the gastro-intestinal tract were striking. The stomach was collapsed, normal in appearance. On opening it was found to contain a small amount of blood. The mucosa was normal. The duodenum was distended and firm, apparently containing a mass within its lumen. On opening a large blood clot forming a perfect cast of the lumen was found. The ampulla



FIG. 1.—Case I. Anterior wall of aorta, showing situation of aneurysm.

was patent. The mucosa was everywhere normal except for two small ulcers on its posterior wall, the first occurring 5 cm. below the ampulla, the second 2 cm. below the first. These ulcers were 1 cm. in diameter, their edges thin, greenish, friable, indicating an acute necrotic process. There was no induration of their edges. The posterior wall in which these ulcers were situated was bulging into the lumen lying directly upon an indefinite mass. The two ulcers were directly connected with this mass. The greater portion of the jejunum was filled with clot similar to that in the duodenum.

The aorta presented the following conditions: There were no marked lesions up to a point 1.5 cm. below the renal arteries. Here its wall was thinned and wrinkled, there being a marked fusiform dilatation involving the part lying between the renal arteries and the bifurcation. The circumference at the level of the inferior mesenteric artery was 4.5 cm.; at the level of the renal arteries 3 cm. The length of the dilatation was 5.5 cm. In the region of the inferior mesenteric artery there was an ulcerated



FIG. 2.—Case I. Duodenum, showing points of rupture in posterior wall.

oval area 3 x 3.5 cm., the long axis horizontal. The tissue at the base of this ulcer was dark brown, friable, mealy. Extending from the edges there were several bright red granulation-like areas. The origin of the inferior mesenteric artery could not be determined. Anterior to this dilatation there was a soft oval mass which pushed forward the posterior wall of the duodenum. Section antero-posteriorly through this mass showed it to be an aneurysmal sac, its walls being in direct continuity with the aorta. Anteriorly in the region of the duodenal ulcers its wall was thinned. This

sac was completely filled with thrombus, so that it was fairly firm. The opening of the aorta into this sac measured about 1 cm. in diameter. Several parallel sections showed that this perforation and the aneurysmal sac were in no way connected with the inferior mesenteric artery, which was found to lie to the left embedded in the mass of fibrous tissue about the sac. This artery was dilated and tortuous in its beginning and completely occluded by thrombus. Histological examination showed the intima of the aorta



FIG. 3.—Case II. Anterior wall of aorta, showing location of aneurysm.

to be hyaline; media hyaline and degenerated. The walls of the sac were fibrous, containing small follicles of lymphoid cells. The sac was filled with thrombus.

CASE II.—This case we are able to report through the interest of Dr. S. B. Wolbaeh who turned over the specimen to us and procured copies of the history and autopsy protocol and permission to report the case from the staff of the Long Island Hospital.

J. T. S., male, aged eighty-one years, entered Long Island Hospital, April 25, 1904. Service of Dr. J. J. Minot.

*Family History.* Negative.

*Past History.* Had measles and pertussis in childhood. Otherwise has always been well.

*Past Illness.* Began nine weeks previous to entrance, with a sharp pain in the small of his back; this laid him up so that he was unable to work. When the pain disappeared he usually felt weak. His back was not stiff, he had extreme pain on rising or sitting. His appetite was poor. His bowels were constipated. He denied venereal disease.



FIG 4.—Case II. Duodenum, showing site of rupture.

*Physical Examination* showed a fairly well-developed, thin, senile man. He had a marked arcus senilis. There was considerable sclerosis of the radial artery. His lungs, heart and extremities were unimportant.

*Abdomen.* In epigastric region, just above the umbilicus, was felt an oval tumor about 3 x 11 inches in size. The tumor pulsated and was slightly tender. Liver not enlarged. Spleen not palpable.

Urine examination negative.

*Course.* May 11, sixteen days after entrance, the patient was in fair general condition. His only complaint was of pain in his

back. During the night of May 12 he fell out of bed, after which he vomited and passed by rectum considerable blood. He felt weak, but his pulse remained low. The following morning he was comfortable. During the night of May 16 he collapsed, apparently having been comfortable up to this time. He did not respond to treatment, but grew weaker, and died within half an hour.

Autopsy was performed ten hours postmortem by Dr. George B. Magrath. The body was that of a man, aged eighty-one years; well developed and fairly well nourished.

The heart showed advanced chronic fibrous myocarditis. The coronaries were sclerotic and dilated in the upper part of their course. The lungs showed emphysema, edema and congestion, chronic tuberculosis, and chronic adhesive pleuritis. The liver, spleen, and pancreas showed no lesions of importance. The kidneys on gross examination showed a chronic nephritis. The prostate was hypertrophied. There was marked general anemia.

The lesion of the gastro-intestinal tract were similar to those found in the first case. The stomach was distended with fluid contents which on section was found to consist of semifluid with partially clotted blood. The largest mass of clot was about 15 cm. in diameter. The mucosa was normal. The duodenum and greater part of the ileum were markedly distended with dark red semifluid, and partially clotted blood. The third portion of the duodenum in the midline projects forward, apparently overlying a vague irregular mass about 7 cm. across. The overlying peritoneum was thickened. Upon section at this point the duodenum presented on its posterior wall an opening  $2 \times 1.5$  cm., which on pressure yielded a small amount of grayish-red clot. The edges of this opening were rounded, somewhat irregular, and drawn downward. Upon further dissection this opening communicated with blood clot, and in continuity with the aorta through an opening in its anterior wall  $4.5 \times 3$  cm., the long axis vertical, the edges rounded and infiltrated. This intervening sac, about 5 cm. in diameter, had on its inner surface a laminated clot. Its cavity was for the most part empty. A probe inserted into the opening in the duodenum entered this cavity obliquely. Adjoining this sac and communicating with the aorta was an oval opening 3 cm. in diameter. To the right of and in continuity with the opening in the aorta already described was another nearly empty cavity, 4 cm. in diameter, lined by laminated clot, bounded in front by the inferior vena cava, behind by the lower lumbar vertebrae, and externally by the psoas muscle. This muscle was pale brown, streaked with yellow, and mottled with areas of necrosis and hemorrhage in its lower and posterior portion.

The aorta, in addition to the aneurysms above described, which lie 4 cm. below the renal arteries, presented marked arteriosclerosis

with dilatation. The circumference at the level of the celiac axis was 6.5 cm.; in the middle of the thoracic segment 8 cm.; at the level of the left subelavian artery 7.5 cm. The inner surface was marked by alternating areas of elevation and depression, the latter calcareous, the former soft in some instances, on section containing a mortar-like substance and overlaid with fragile thrombi. Many of these areas were ulcerated. The inferior mesenteric artery was embedded in a mass of firm, fibrous tissue to the left of the aneurysmal sac. On section it was found completely thrombosed, its point of origin to the left of the opening in the aorta.

DISCUSSION. It is interesting that these two cases should be so nearly alike both in their clinical and pathological features. The situations and points of rupture are identical. The same etiological factor is present in each case. Arteriosclerosis as the basic cause in the first case may seem questionable, but the lesions are characteristic, both grossly and microscopically. Furthermore, the clinical findings are against syphilis, the heart condition against an embolus as the primary cause. The etiology in the second case is beyond doubt, owing both to the age of the patient and the character of the aorta.

To account for the history of a month's duration of hemorrhage in the first case there is no definite pathology. Undoubtedly what occurred was that the throbbing pressure of the aneurysm upon the duodenum first wore a small perforation through the intervening walls, which was plugged easily with clot after some hemorrhage. The constant throbbing force, however, made it impossible for complete repair to take place, but rather to hinder it, and at the same time to destroy more of the limiting wall, so that the perforation finally became so large and the flow of blood through it so rapid that no clot could form and check the hemorrhage into the duodenum. In support of this is the fact that the edges of the ulcers were acutely necrotic, containing no evidence of scar formation.

In the second case the severe pain in the back can be explained by the pressure on the necrotic psoas muscle. In this case the walls intervening between the duodenum and sac were thinner than in the first case, so that when the rupture took place a larger opening resulted, with a more acute exodus.

In conclusion we would summarize that these two cases are cases of aneurysm of the abdominal aorta apparently of arteriosclerotic origin which ruptured into the duodenum.

We owe many thanks to Dr. Christian and Dr. Goodpasture for permission to report the case which occurred in this hospital, and to Dr. J. J. Minot for the opportunity and permission to report the second case, which occurred in the Long Island Hospital.

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## RELATION OF CONGENITAL SYPHILIS TO MENTAL DEFICIENCY.<sup>1</sup>

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THE general practitioner seldom receives a more unwelcome visitor than the mentally deficient child. The failure of the usual lines of treatment and the hopeless prognosis are too well known for discussion.

It is conservatively estimated that there are 5000 defective children in the State of Virginia. This number, of course, does not include the borderline cases nor the so-called latent types of enfeeblement. Those who have studied the problem most deeply, and who are best able to recognize the moron, usually consider that about 2 per cent. of the school population is feeble-minded, and the larger part of these belong to the high-grade class. It is generally conceded that of these 80 per cent. spring from families in whose lineage similar types may be found.

Naturally, syphilis has been considered as a possible causative factor for many years. In 1888 Shuttleworth examined 1000 cases of mentally deficient children by clinical methods alone and found evidences of syphilis in only 10. Others following him reported similar experiences. Even so recent a writer as Goddard<sup>2</sup> states that if ever syphilis produces feeble-mindedness, it does so only under most favorable conditions. Contemporaneous with this statement, Nonne<sup>3</sup> found syphilis affecting the nervous system in less than 2 per cent. of his series of 1000 cases of nervous diseases.

More recent studies, however, have absolutely established the predisposition of the *Treponema pallidum* for nerve structures.

<sup>1</sup> Read before the Medical Society of Virginia at its Forty-seventh Annual Session, held at Norfolk, Va.

<sup>2</sup> Feeble-mindedness; its Causes and Consequences, New York, 1914.

<sup>3</sup> Syphilis and the Nervous System, 1913.



Since the valuable contributions of Ravant,<sup>4</sup> Altman,<sup>5</sup> Gennerick<sup>6</sup> and others it is now well known that the spinal fluid is involved early in practically every specific infection. In fact, with the almost universal dissemination of the infectious agent it is difficult to conceive how any organ escapes the infection.

With such a direct relationship existing between acquired syphilis and the central nervous system the frequency of congenital syphilis manifesting itself in its points of predilection should be of vital interest to us. The method of transmission of the spirochete from parent to child has been the subject of discussion for a number of years. Suffice it to say that in the light of our present knowledge the weight of evidence favors maternal transmission. Thus the offspring becomes directly infected with the organisms circulating in its blood. It is important to know that the inheritance of syphilis may take place, although the parental infection has occurred many years before. Nonne<sup>7</sup> quotes a case of Fournier's in which the interval was fifteen years. It may manifest itself in early life in accordance with the usual signs, or the child may escape and later become a victim of the so-called latent or tardy stage.

The pathology in no way differs from that found in acquired infections. The disease may implicate the bloodvessels, meninges, or parenchyma. However, owing to the proximity of these structures and the protean manifestations of the organism it is not likely that one part would be involved without the others showing in the pathological process. The severe forms of restrictive development of the central nervous system are very important and to a certain extent characteristic of congenital lues. According to Nonne, malformations of the brain and cord not infrequently occur, as well as developmental deficiencies in the peripheral nerve roots. Jarisch has demonstrated at autopsy an actual decrease in the number of ganglion cells, a change in the protoplasm of the cells, and vitreous masses around the bloodvessels in the central nervous system. In a comprehensive report of 100 cases of late syphilis, Veeder<sup>8</sup> found lesions of the nervous system in 47, or approximately one-half. Of these 23 were mentally deficient, 14 had cerebrospinal syphilis, and the remaining were divided among less frequent nervous conditions.

There may be a second way by which syphilis may affect the offspring. Quoting from Haberman:<sup>9</sup> "Such parents are themselves constitutionally affected by the disease, and hence the germ cells uniting to form the embryo may also, one or both, be affected, depleted or invalidated, just how cannot be said. The fact remains that this embryo, without containing the infective organism itself, enters from the start on a darkly checkered career whose fate may

<sup>4</sup> Quoted by H. F. Swift: *AM. JOUR. MED. SC.*, 1916, clii, 490.

<sup>5</sup> *Ibid.*

<sup>6</sup> *Ibid.*

<sup>7</sup> *Loc. cit.*

<sup>8</sup> *Am. Jour. Dis. Child.*, 1914, viii, 283.

<sup>9</sup> *Jour. Am. Med. Assn.*, 1915, lxi, 1141

be almost as sinister as that of the really infected embryo." Such children will give no Wassermann reaction. They are not syphilitic but are neuropathically or psychopathically marred. Although this *modus operandi* is open to question it may seem to explain the negative Wassermann reactions sometimes found in the defective children of syphilitic parents.

The first important contribution bearing on the relation of congenital syphilis to mental deficiency was in 1914 by Fraser.<sup>10</sup> In 99 feeble-minded children she found positive Wassermanns in 44.9 per cent. In only 8 of her series were any clinical signs of syphilis present. About the same time Watson<sup>11</sup> in an examination of 204 cases found that 60 per cent. gave a positive reaction. According to some investigators, serological tests of the entire families in which defective children appear show that syphilis is associated with a still higher percentage of cases than is ascertained by the examination of the patient alone.

In Gordon's<sup>12</sup> series of 75, which he studied especially from the stand-point of hereditary syphilis, mental defects of various degrees were present. He found a positive Wassermann in 50 per cent. of his cases. The spinal fluid was examined in 17, all of which reacted positively, with the exception of 3 cases of feeble-mindedness associated with functional nervous disorders.

The object of this paper is to report the results of the serological studies on the first 50 cases admitted to the psychological clinic of the Medical College of Virginia during the past year. The material for this clinic is drawn largely from the retarded classes of the Richmond Public schools, the juvenile court, and other agencies interested in the social welfare of the city. They were sent for the purpose of obtaining the estimate of their mental development as well as a clue to any factors influencing their mental and moral stamina. In addition to the usual physical and neurological examinations, various psychological tests were employed, the results of which are obviously unnecessary in this review. In this series 21, or 42 per cent., gave a positive Wassermann reaction. Their ages varied from seven to sixteen years, and with the exception of 1 all were white. In the accompanying chart of the positive cases the mental level obtained by the Binet-Simon questionnaire, general health, physical defects, and type of temperament are noted. It will be seen that the series is composed largely of the middle and high-grade imbecile and only exceptionally with the low-grade idiot. This in part may account for the relatively low percentage of Wassermanns found in institutions for the feeble-minded. With two exceptions the general health of the children was uniformly good, a fact which made it difficult for us to impress upon the families the necessity for persistent treatment.

<sup>10</sup> Jour. Mental Sc., October, 1913, p. 234.

<sup>12</sup> Gordon: Arch. Pediat., 1916, xxxiii, 273.

<sup>11</sup> Ibid.

Quite at variance with other reports is the striking relative absence of congenital syphilis or organic lesions of the nervous system. Approximately one-half showed a general glandular enlargement. Defects of vision, tonsils, etc., were found no more frequently than in the non-luetic series. The most interesting and suggestive physical aspect was the malformation and caries of the teeth. One of three types were present in each of our cases. The most frequent form was the small, widely separated teeth, with well-marked serrations on the upper and lower incisors. This was associated with moderate caries, especially about the neck of the tooth. The second type was similar to the first, but with a much more advanced grade of dental infection. The least common type was the usual set of teeth riddled with areas of decay. In only 2 of the 21 cases were the teeth even approximately normal. No typical Hutchinson teeth were observed.

Temperamentally the series presented an interesting picture; 14 of the 21 were either incorrigible, disobedient, or displayed fits of temper unlike those usually seen in the normal child. Although our series is too small from which to draw definite conclusions, we are not disposed to feel that the listless, low-grade idiot is so likely to be of syphilitic origin as the high-strung, passionate child with wayward tendencies. It has been shown that the percentage of positive Wassermanns is materially lessened after the sixteenth year.

The recognition of syphilis as a factor in the production of mental enfeeblement is of the uttermost importance in their proper handling and treatment. According to Gordon, where gross malformations do not exist, encouraging therapeutic results are obtained. Nonne<sup>13</sup> speaks of various organic and functional nervous disorders in children with inherited syphilis who improved and some recovered after antisiphilitic treatment. Fournier, likewise, has reported satisfactory results in the treatment of the vague nervous and psychic disorders of congenital syphilitic origin.

If it can be established that inherited syphilis is a frequent factor in the production of the subnormal mentalities the problem of the feeble-minded will present a more hopeful outlook. Recalling the pathology of syphilitic lesions of the brain, it is useless to hope for an amelioration of symptoms in those cases in which the process is long-standing or is destructive in character. Therefore the early recognition of the condition is imperative and our attention should be directed more especially to those borderline types in which mild mental defects are associated with moral delinquencies. It must be borne in mind that the syphilitic organism can be readily transmitted to the third generation and that only a very small percentage of congenital syphilitics can be recognized by clinical methods alone, and no study of an enfeebled child should be considered complete without a Wassermann test. If a negative result is obtained, further

inquiry and examination should be made of the parents and other members of the family. Should we be able by this means to reclaim even a few of those destined to become a burden to society and the State our efforts will not have been in vain.

No.	Age.	Mental age.	Years back.	General health.	Physical defects.	Temperament.
1	12	7.6	4.4	Negative	Teeth and ears	Sensitive.
2	16	10.0	6.0	Negative	Teeth	Sexual pervert.
3	11	6.2	5.0	Negative	Internal squint	Incorrigible.
4	15	10.0	5.0	Negative	Teeth	Sullen.
5	12	8.2	4.0	Negative	Glands	Incorrigible.
6	8	4.2	4.0	Negative	Teeth; glands; squint	Incorrigible.
7	7	4.1	3.0	Negative	Teeth	Incorrigible.
8	10	5.2	5.0	Negative	Teeth	Listless.
9	11	7.2	4.0	Negative	Teeth; glands	Disobedient.
10	12	10.0	2.0	Negative	Negative	Incorrigible.
11	14	10.0	4.0	Negative	Negative	Incorrigible.
12	15	10.0	5.0	Negative	Glands	Slow.
13	12	10.0	2.0	Headache	Glands	Temper.
14	14	7.3	6.7	Negative	Heart glands	Incorrigible.
15	11	4.0	7.0	Headache	Teeth; ears	Listless; incorrigible.
16	14	10.4	3.6	Negative	Glands; teeth	Incorrigible.
17	8	6.3	1.7	Negative	Glands; teeth	Slow.
18	11	7.2	3.8	Negative	Teeth	Slow.
19	15	10.8	4.2	Negative	Teeth; speech	Sullen.
20	10	5.0	5.0	Negative	Teeth; glands	Sex; habits; incorrigible.
21	16	8.0	8.0	Negative	External squint and teeth	Slow and sullen.

## MULTIPLE SEROSITIS; REPORT OF A CASE WITH AUTOPSY FINDINGS; DISCUSSION OF ITS CLASSIFICATION.

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SINCE the publication of the interesting and exhaustive monograph of Kelly on this subject in 1903, very little has appeared in medical literature in reference to the condition known as chronic obliterative pericarditis with ascites.

Chronic perihepatitis, associated with varying degrees of chronic inflammation of the pericardium and pleuræ, as a local manifestation of diffuse chronic peritonitis has been recognized for more than half a century. Rolleston restricts the name multiple serositis to this condition, and includes in this category the chronic hyperplastic perihepatitis described by Curschmann in 1884 and called by him Zuckergussleber, sugar-iced liver, so-called from the thick encasement of fibrous connective tissue, more or less enveloping the liver, whitish, glistening, somewhat resembling confectioners' icing.

In 1896 Pick described, under the term "pericarditic pseudo-liver cirrhosis," three patients whose ailment was predominantly ascites of long duration together with enlarged liver, but at autopsy in each instance showed thickened and obliterated pericardium not suspected during life. Two of these cases presented some degree of liver cirrhosis, not in proportion, however, to the amount of ascites present, the other an enlarged nutmeg liver, the cardiac liver of the French writers. All of these cases presented marked perihepatitis. This communication became the subject of much discussion at the time, and the condition described has since been frequently called Pick's disease, though, as mentioned before, it was known to earlier writers.

Rolleston distinguishes the condition described by Pick from the cases of perihepatitis which he considers as only a local manifestation of diffuse chronic peritonitis, in that the former presents primarily an extreme grade of chronic venous engorgement of the liver dependent upon the cardiac condition, the peritoneal thickening or adhesions that may occur being incidental. Thus we have portrayed two more or less distinct clinical pictures: the so-called Pick's disease, in which the predominating condition is the nutmeg or cardiac liver, characterized by chronic venous engorgement, later by red atrophy, and ultimately cirrhosis; on the other hand, those cases of multiple serositis in which the perihepatitis is the prominent clinical feature. Both conditions present at autopsy pericardial lesions, though this condition may not have been apparent during life.

Much confusion has naturally arisen through this rather delicate distinction.

Kelly, in 1903, attempted a broader classification, and grouped under the name multiple serositis those cases "characterized clinically by marked ascites, with little or no edema of the legs, cases in which the diagnosis of cirrhosis of the liver is usually made and which at the necropsy reveal chronic obliterative pericarditis and certain morbid changes in other tissues and organs, notably pleuritis, peritonitis, perihepatitis, nutmeg liver, red atrophy of the liver, cirrhosis of the liver, etc."

In the monograph the author has gathered from the literature 39 cases which he has tabulated with reference to symptomatology and autopsy findings. A complete bibliography on the subject up to 1903 is appended, to which the reader is referred.

It is of interest in the present discussion to report the following case, the clinical notes for which I am indebted to my intern, Dr. M. J. Price:

C. J. D., single, male, aged fifty-four years, a native of Panama, was admitted to my service at St. Luke's Hospital, June 22, 1916, complaining of cough, increasing dyspnea on exertion, and swelling of the extremities, which had lasted for the last nine months.

There was nothing of importance in his family history.

The patient's general health had never been very good, and as a child he was subject to frequent colds. Had never been subject to sore throat. At the age of eighteen he had an acute attack of inflammatory rheumatism, involving all the joints, and persisting for a period of three months. There had been no recurrence of these symptoms. Fifteen years ago he was confined to his bed for six weeks with typhoid fever, making an uneventful recovery.

*Respiratory System.* Has been subject to frequent colds, but denies pain in the chest, hemoptysis, and night-sweats.

*Cardiovascular System.* Nothing abnormal up to nine months ago.

*Urinary System.* Denies dysuria, polyuria, and nycturia.

*Sexual System.* Single; denies Neisser and luetic infections.

*Neuromuscular Systems.* Nothing abnormal.

*Weight.* No recent change in weight; 114½ pounds.

About September, 1915, patient noticed that he was gradually becoming short of breath on the slightest exertion. This symptom gradually increased and was accompanied by swelling of the extremities. Within the next month the patient developed a severe, fatiguing cough, which has lasted up to the present time.

During the month of January, 1916, patient was very ill and weak. The distressing symptoms at that time were shortness of breath, swelling of the ankles, and a severe dry cough. Last week he was seized suddenly with a temporary paralysis involving both extremities and was unable to use them for the greater part of a day.

Man of medium build, five feet five inches tall, dark complexion, and of fair development and nourishment.

Condition of the mouth unhealthy; many diseased teeth and considerable pyorrhea. No noticeable abnormalities of nose, ears, and throat.

The cervical glands are palpable and small. No palpable enlargement of the axillary and clavicular glands.

*Heart.* The apical impulse is visible 13.5 cm. from the median line. The heart sounds are indistinct and muffled; the pulmonic second sound is accentuated. There are no murmurs. Peripheral arteries do not appear thickened.

*Blood-pressure.* Systolic 120, diastolic 90, pulse rate 90.

*Lungs.* The excursion of the diaphragm is diminished on both sides. There is hyperresonance over both lungs to the fourth ribs, from there down dulness or flatness on both sides, shifting somewhat on change of position of the patient. Auscultation reveals a few crepitant and sonorous rales above the areas of dulness. Vocal resonance and tactile fremitus are absent over these areas and the breath sounds are faintly heard. Posteriorly dulness corresponds with that in front, with similar signs on auscultation. Respirations 24. Roentgen-ray examination confirms the physical findings, but

shows in addition a heavy right hilus shadow and a dilated descending aorta.

*Abdomen.* The abdomen is symmetrical and there are no areas of tenderness or rigidity. The hepatic dulness extends from the fifth rib and is just palpable at the costal margin. The edge is smooth. The spleen is not palpable and by percussion seems of normal size. There is a small amount of ascitic fluid.

*Extremities.* Marked pitting edema of both feet and legs. The finger-joints show evidence of hypertrophic arthritis.

*Genitals.* No apparent abnormalities.

*Skin.* A peculiar brownish maculopapular eruption is present in the clavicular fossæ, and on the right thorax a similar eruption follows irregularly the course of the seventh intercostal nerve.

*Urine.* Scanty, sometimes turbid, traces of albumin, indican in excess, with hyaline and occasional granular casts. Kidney function as shown by the phenolsulphonephthalein test practically normal. Blood findings negative, except for a slight increase in the leukocytes (12,430) with a relatively high lymphocyte count. Blood serum presented a negative Wassermann. The sputum, scanty in amount, reveals no tubercle bacilli on repeated examinations, though it contains various other bacteria and several herzförmige Zellen. Cutaneous and intracutaneous tuberculin tests were negative.

He remained in the hospital until the time of his death, about one month later. The edema in the legs promptly went down following rest in bed, and the dyspnea and cough improved. Thoracentesis was done three times and considerable amounts of fluid aspirated, once from the right and twice from the left pleura. Removal did not affect the position of the apex beat, nor was it changed on change of posture of the patient. Following the removal of 650 c.c. of fluid from the right pleura obliteration of the cardio-hepatic angle was demonstrated. The fluid removed was slightly turbid, not bloody, and was negative to cultures and guinea-pig inoculations.

The urine was persistently low in quantity, though at first much increased by the administration of theocin.

He became progressively weaker, was very nervous and restless the last few days of life, and died in an attempt to get out of bed.

*Clinical Diagnosis.* Chronic pleurisy; chronic pericarditis, with effusion; pericardiopleural adhesions; probable chronic peritonitis.

*Autopsy.* July 29, 1916. Made by Dr. E. V. Knapp, the hospital pathologist, showed the following:

Man about forty-five years old; dark complexion.

Pupils dilated and equal; no jaundice; visible mucous membrane pale.

Teeth poorly kept.

Marked emaciation; no edema.

Dark brown pigmented areas over lower abdomen and lower thigh and over side of chest, especially the right; no infiltration or induration. Over the lower thighs, patellæ, shins, forearms, especially the back, there are numerous pustules, about 2 mm. in diameter; dark brown induration around them; center is depressed, slightly indurated, somewhat shotty. None on soles of feet or palms, none on chest or face. Pigmented areas scattered over buttocks and lower lumbar region. No glandular enlargement except inframandibular, which are hard and shotty.

Median incision shows a moderate amount of fat of good color; the blood is bright red. Cartilages and muscles are of good color. There is a large amount of slightly turbid, blood-tinged fluid in the abdominal cavity.

The diaphragm is at the fifth intercostal space on each side.

The liver is about four finger-breadths below the costal margin in the midclavicular line on the right side. The left lobe is about three finger-breadths below the costal margin in the midclavicular line. The notch is well marked.

The intestines and omentum are slightly congested.

There are no abnormalities of the sternum.

Both pleuræ contain a large amount of hemorrhagic fluid.

The lungs are somewhat atrophic; there are no adhesions at the right apex; there are many adhesions at the left apex and hilus, also posteriorly. There are many fibrinous adhesions at the right upper and lower lobes attached to the pericardium.

The pericardial sac is filled with a considerable amount of straw-colored fluid. There are numerous pleuropericardial, mediastinopericardial and phrenopericardial adhesions. The thoracic wall is smooth.

The right lung shows many interlobular fibrinous adhesions. The surface of the right lung is moderately smooth; there is a moderate amount of dark brownish pigmentation. There are no adhesions or scars at the apex. In the upper lobe, anteriorly, there is a hard, indurated smooth mass about the size of a small hen's egg. Middle lobe is free, with the exception of a small nodule. At inferior lobe there is a hard, nodular, indurated mass, about the size of a lemon, somewhat hemorrhagic. On cut section this mass is glistening and dark red in color and definitely outlined. Other nodules are similar. The pulmonary vessels are clear.

The left lung shows many fibrinous adhesions at the apex and upper margin of the lower lobe; surfaces are smooth; the left lower lobe is congested and indurated and of a dark muddy color. The cut surface appears deep red; is only slightly crepitant.

Amount of fat about the heart is moderate; the muscle tissue is flabby, somewhat pale, and brownish; surfaces are smooth. The aortic valve is slightly roughened but shows no vegetation or calcification. Other valves are normal. The left ventricular wall is about 3 cm. thick, the right about  $\frac{1}{2}$  cm. thick. Trabeculæ are



hypertrophied. There is no sclerosis in the coronary arteries. The pericardium is smooth, thick, and glistening; there are no adhesions to the myocardium.

The heart is about 18 cm. across at the base, 16 cm. from base to apex, and about 10 cm. through.

There are many adhesions between the left lobe of the liver and the lesser curvature of the stomach, between the right lobe and the diaphragm and between the right lobe and transverse colon. The gall-bladder is normal in size. The liver is about 24 x 15 x 10 cm. The surface is smooth; the cut surface has a brownish, mottled appearance; the lobules stand out very distinctly. There are no areas of induration or nodules. The liver capsule is somewhat thickened.

The lower pole of the spleen is at the eighth rib in the axillary line. There are a few adhesions between the spleen and the greater curvature of the stomach. The spleen is about 10 x 7 x 4 cm., of a grayish-slate color. Cut section shows the trabeculae well marked, the pulp pale.

The right suprarenal is pale yellow, flabby, but there is no evidence of tuberculosis. The left is normal in size and the surface is slightly nodular.

The kidneys are normal in size and the capsule stripped easily. The right shows the cortex somewhat congested and a small scar at the lower portion, anteriorly, about the size of a pea. The left presents six small cysts, each about the size of a pea, which contain a clear yellow fluid. At the lower middle portion there is a depressed scar about the size of a dime. There is some atrophy of the cortex; the glomeruli and tubules are prominent.

There are many adhesions between the pancreas and the upper part of the stomach and duodenum. It is normal in size and appearance.

The stomach is normal in shape and position. There are a great many adhesions to the surrounding organs; the omentum is normal.

The appendix is normal and retroverted.

There are many adhesions binding the transverse colon and the upper intestines.

The lower large bowel is firmly adherent.

There are no areas of induration in the lower rectum.

The prostate is small and fibrous.

The anterior and posterior surfaces of the bladder are firmly bound to the surrounding tissues by dense bands of fibrinous tissue.

There are a few scattered yellowish plaques in the upper portion of the aortic arch.

*Histological Examination.* Sections of the spleen show normal markings. There is a slight interstitial thickening of the pulp.

Sections of the liver show a slight thickening of the periportal connective tissue. There is slight cell infiltration around some of

the bile capillaries. The capsule also shows slight connective-tissue thickening. There is a considerable amount of fat in the periphery of some of the lobules in the form of small and large droplets in the liver cells. Near the centers of the lobules the liver cells are small and contain much fine, brownish pigment.

Sections of the lungs show in places marked hyperemia. Many of the air spaces are filled with erythrocytes and desquamated epithelium. Another section of the lung shows an area in which the air spaces are filled with blood. Around this area is a marked hyperemic zone.

Sections of the pancreas are normal.

Sections of the heart muscle show areas of intense cell infiltration, with leukocytes and partly organized blood clot.

Sections of the suprarenals are normal.

Sections of the kidneys show numerous scars in the cortex. There is a moderate amount of fibrinous thickening in the straight tubules. Many waxy and granular casts in the tubules. There is a small pyramidal area in the cortex in which the glomeruli and some of the tubules are apparently necrotic.

Sections of the skin in the region of a pustule show no evidence of inflammation, but the epithelium and subcutaneous tissues are entirely necrotic.

*Anatomical Diagnosis.* Polyserositis. Pleurisy with adhesions. Pericardiophrenic (pleural) and mediastinal adhesions. Pericardial effusion. Chronic peritonitis. Adhesions of bladder, intestines, pancreas. Myocardial hypertrophy and degeneration. Chronic congestion of liver. Beginning cirrhosis. Arteriosclerosis involving aorta and kidneys. Pulmonary infarction.

While the case here recorded presents the widespread disease of the serous membranes which justifies the diagnosis of multiple serositis, a critical analysis of the clinical course and the autopsy record makes it at once apparent that it presents features somewhat at variance with the descriptions of other investigators.

Ascites was not a prominent condition. While it was demonstrable at examination and a considerable amount of fluid was found at autopsy, it had not been in such amounts as to require tapping for its relief, and could scarcely be said to fall within the classification requirements of Kelly, who describes marked ascites as the striking clinical feature in all of the 39 cases reported by him. That the degree of ascites will vary dependent upon the pathological condition of the liver is certain. Chronic venous engorgement of the liver is present in a majority of these cases, though cirrhosis is found in some. It is questionable upon what the ascites depends. The sequence of appearance of the pathological features is uncertain. It is open to question whether the ascites is produced by the chronic portal obstruction dependent upon the venous engorgement of the liver or whether a chronic peritonitis caused by portal and peritoneal engorgement is responsible for it.

Again, the perihepatitis, marked in a majority of the cases reported, particularly if it leads to compression of the liver and the portal radicles, produces an important factor contributing to ascites. The clinical history of these patients throws little light on the organs or tissues first affected in multiple serositis. Pick considered the obliterative pericarditis the primary condition and sought to establish an etiological relationship between it, the enlarged liver, and the ascites.

*Chronic Obliterative Pericarditis.* This condition next to ascites is the most constant. It was present in all of the cases presented by Kelly—complete obliteration in the majority of them. It was present in all of Pick's cases. Other writers, however, have not found it constant. Rolleston, who makes a sharp distinction between pericarditic pseudocirrhosis of the liver (Pick's disease) and multiple serositis, admits its frequency in the latter disease, but does not assume its importance as the primary pathological factor. Picchini found the pericardium involved in only 9 of 50 cases observed by himself.

There were no adhesions between the pericardium and cardia in the case presented by the writer. There was pericardial effusion. The ravages of inflammatory disease of the pericardium were, however, marked by numerous adhesions of the pericardium to the mediastinum, pleura, and diaphragm. The etiology responsible for these cases of pericarditis obliterans is rather obscure and the antecedent pathology is frequently uncertain. As long ago as 1837 Laennec called attention to the fact that the adhesions followed the absorption of pericardial effusion. In all probability obliterative pericarditis has been given too great significance as the factor in the production of the disease, and the role played by the weakened cardiac muscle has been overlooked. Adherent pericardium may exist symptomless for years. Myocardial weakness, however, dependent upon or coincidental with it, is responsible for the venous congestion of the liver with its resulting chronic portal obstruction, ascites, and peritonitis.

Chronic perihepatitis is constant, varying from a slight connective-tissue thickening of the capsule, as described in the writer's case, to the Zuckergussleber of Curschmann, where the liver is encased in a coating of fibrous tissue of cartilaginous consistence. The importance of perihepatitis as the primary pathological factor on which the widespread involvement of the serous membranes depends has been advanced by some investigators.

Of interest here is the association of chronic perihepatitis with arteriosclerosis and granular kidney. Hale White, quoted by Rolleston, found it present in 19 out of 22 cases. There appears to be some connection between arteriosclerosis and fibrosis of the serous membranes. Rolleston admits that arteriosclerotic change in the kidney may be a disposing cause of chronic inflammation in the body generally by reducing the bactericidal power of the blood.

In the case here recorded sclerotic plaques were found in the aorta, and the kidneys showed numerous arteriosclerotic scars in the cortex.

Of interest in this case were the multiple infarcts found in the right lung, two of them of considerable size. This condition has not been heretofore observed in the literature on the subject. It may have accounted for the extreme restlessness and dyspnea which were present before death. Unfortunately no cultures were made.

The cause of multiple serositis is obscure. The tendency to attribute to the tubercle bacillus the role of the etiological factor in chronic pericarditis and chronic disease of serous membranes generally is altogether too prevalent. That tuberculosis is often the cause and that tuberculous lesions are frequently found associated with this condition is undoubtedly true. That evidence of a tuberculous infection can be seen at most autopsies is equally true. No evidence of tuberculosis was found in any of the organs of the case here recorded, nor was there anything in his history suggestive of antecedent tuberculous infection. Of significance, however, was the history of acute rheumatism which he had when eighteen years of age, and which lasted for a period of three months, though he had no subsequent attacks. The case reported by Kelly presented a similar history, and he emphasizes the etiological importance of rheumatism.

There would seem to be considerable confusion among writers concerning the classification of this interesting condition, of which multiple serositis seems to be the one constant feature. This would appear to be largely because certain pathological conditions have been somewhat arbitrarily presented as fundamental to the production of the group of lesions making up the clinical entity. That the microbic invasion responsible may attack any of the structures involved must be conceded. It would therefore appear that until further investigation presents more light on the etiological factor or factors causative that a broader classification would be desirable and that multiple serositis should not be restricted to a clinical picture necessarily associated with adhesive pericarditis or perihepatitis, which, after all, are probably but conditions incident to the general serous involvement rather than responsible for it.

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## THE ESTIMATION OF UROBILIN AND UROBILINOGEN IN THE DUODENAL CONTENTS.

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IN a study of diseases associated with evidence of increased blood destruction it is desirable to attempt to estimate the activity of hemolysis and to compare this with the probable capacity for blood regeneration. Many workers have used as an index of blood destruction the changes that occur in the contents of the bile, namely, the amount of bile pigment excreted, and especially the amount of urobilinogen and urobilin. Eppinger estimated the amount of urobilinogen and urobilin in the stools by means of the Charnas spectrophotometric method and stimulated interest in this manner of estimating blood destruction, particularly in pernicious anemia and hemolytic icterus. In this country a more simple procedure for making rough quantitative estimates of these substances has been devised by Wilbur and Addis. Robertson, making use of the method, has reported findings in every way comparable to those of Eppinger.

The theories advanced with regard to the fate of hemoglobin after hemolysis are not well substantiated. Recent investigations by Whipple and Hooper are especially important. Their experiments involved a great deal of careful study over a considerable period of time, and, of necessity, only on dogs. Their conclusions are in some respects iconoclastic. If further work substantiates their findings it may be necessary to change our conception of the factors concerned in the formation of bile pigment. These authors conclude, especially from their results regarding the influence of diet on bile-pigment production, that the disintegration of red blood cells is not the important factor in the production of bile pigments. They have made estimations chiefly of the amount of bilirubin. It will be interesting to learn of their results with respect to urobilin and urobilinogen, for in the clinical studies on the hemolytic anemias there is now considerable evidence from many observers that the amounts of these substances excreted are definitely increased. This increase, it is true, may be the result of impaired organ function as well as of blood destruction. The quantity of bilirubin does not, however, run parallel to the quantity of urobilin and urobilinogen in pathological conditions.

In our own studies we have made use of the modifications of the Wilbur and Addis methods recently devised and reported by

Schneider. The essential advance in technic is the application of the observations, not to stool extracts, but to the contents of the duodenum as collected by means of an Einhorn tube. In this liquid an amount of the biliary pigments and their derivatives sufficient for quantitative determinations is readily obtained in a short time. While an estimation of the amounts of these pigments in the duodenal contents at a given time cannot be regarded as an index of the total amount excreted in twenty-four hours, objections are also advanced with respect to the values obtained in the twenty-four-hour stool in which some proportion of the substances may be destroyed or changed in character. The values obtained by Schneider's method have been so definitely in accord with the clinical manifestations that there is little doubt of the existence of a relationship which it is to be hoped may be made clearer by further study. These values are also in accord with the results obtained from estimations on the stool. The technic we have used, which in all of its essentials is that described by Schneider, is presented in detail, in order that it may be readily understood and easily followed. We wish to express our indebtedness to the originator of this method for his personal interest in our work.

#### THE METHOD OF OBTAINING THE DUODENAL CONTENTS.\*

The tube and the metal capsule employed are similar to those of the Einhorn duodenal tube, but experience has led to the use of a somewhat stiffer tube and a capsule which, though similar in shape, is slightly larger and heavier, weighing 6.4 gm. This model of capsule was recommended by Schneider. However, an ordinary Einhorn or a Rehfuß bucket may be used. For convenience in observing the contents of the tube a piece of glass tubing is inserted at its end.

In the preparation for the examination the patient is instructed to partake of no food for at least twelve hours, except perhaps a little tea or coffee without cream, and to take frequent sips of warm water up to the time of the examination. The nature and purpose of the test are also explained, as the patient's confidence and coöperation aid in the passage of the tube.

The passage of the duodenal tube is a simple procedure. The metal capsule is placed on the back of the tongue and the patient is directed to swallow hard several times in rapid succession. There is usually some difficulty as the capsule reaches the level of the cricoid, but this is overcome by deep breathing. After the capsule has passed this irritable zone, peristalsis carries it along without further discomfort to the patient and largely beyond his control. He merely swallows from time to time, taking a few sips of warm water and the capsule finally reaches the stomach and comes to rest at about 60 cm. from the incisor teeth.

\* Described by Szlapka.

The patient is now made to lie on his right side, with the hips elevated eight or ten inches. The pyloric end of the stomach thus becomes more dependent, and gravity, aided by gastric peristalsis, causes the capsule to pass through into position in the duodenum—some 70 cm. from the incisors. In our experience this is accomplished in from fifteen minutes to an hour, usually in about forty-five minutes. At no time is it necessary to push the tube on its way. Pushing only tends to coil it up in the stomach and may even frustrate its passage into the duodenum.

With the patient on his side the end of the tube is allowed to hang well over the edge of the table. Gastric contents siphon out first, the siphon being started by the injection of a few cubic centimeters of warm water. As the capsule moves through the pylorus into the duodenum the fluid recovered becomes yellowish and finally a clear bile is obtained. It may vary in color from light yellow to chocolate brown. Pure duodenal fluid is faintly alkaline, clear, of quite uniform color and viscid; the foam is golden. The liquid must be alkaline. Its mere appearance is not a safe guide as to its identity, although with experience one may come to recognize it readily. The character of the fluid collected must be observed closely, as from time to time the pylorus permits the passage of gastric contents into the duodenum. This impure liquid may be detected by its change in color and its dull, cloudy, opalescent appearance, diminished viscosity, more rapid flow, and change in reaction to litmus or Congo red. It should, of course, be discarded.

Should the flow of bile become interrupted an unusual length of time, the injection of a little warm water into the tube or the taking of deep breaths by the patient, will help to reestablish it. The application of suction is neither necessary nor advisable.

It is our custom to collect the duodenal contents in a small, amber-colored bottle, as air and light cause the rapid transformation of the urobilinogen into urobilin; 20 c.c. of liquid are necessary for the test, which should be made immediately.

#### LABORATORY TECHNIC.\*

The duodenal contents is poured into a graduated cylinder as soon as it is brought to the laboratory, and its gross appearance noted. Normally it is a light, straw-colored, viscid fluid, and this is reported as normal yellow (N). The color may vary to dark yellow, brown, and chocolate. The dark-colored fluids always yield much bilirubin, but the color of the duodenal contents does not always indicate the amount of urobilinogen or urobilin present, as these derivatives of bilirubin are sometimes demonstrated in considerable amounts in normal yellow fluids. Occasionally, however, in cases other than pernicious anemia or hemolytic icterus a colorless, watery secretion with no biliary pigments or derivatives is collected.

\* Described by Sanford.

When 20 c.c. or more of clear duodenal contents is collected it is divided into two 10 c.c. portions in 25 c.c. graduates. To one 10 c.c. portion is added an equal amount, 10 c.c., of a saturated alcoholic solution of zinc acetate (Schlesinger's solution).<sup>\*</sup> The mouth of the graduate is closed by the thumb and the contents thoroughly mixed by vigorous shaking for about one minute. The mixture is then filtered through a single layer of coarse filter paper, the filtrate being collected in another clean, dry graduate. When exactly 10 c.c. of filtrate is obtained it is used for testing for urobilin and urobilinogen. To this mixture, which consists of 5 c.c. of duodenal contents and 5 c.c. of Schlesinger's solution, is added exactly 1 c.c. of Ehrlich's aldehyde reagent<sup>†</sup> measured with a 1 c.c. pipette. The color of the fluid is usually significant when viewed by transmitted and reflected light. If urobilinogen is present in considerable amount, especially if it predominates, the fluid, on the addition of Ehrlich's reagent, becomes a cherry red, varying in intensity with the amount of chromogen present. When there is a preponderance of urobilin the color by transmitted light is yellow or brown, and by reflected light a green fluorescence characteristic of mixtures of urobilin with zinc salts is noted. The graduate is now set in the dark for fifteen minutes before it is examined spectroscopically. This length of time seems necessary to sufficiently sharpen the absorption bands of the spectrum, while if the mixture stands for longer intervals of time some of the mother substance, urobilinogen, may become converted into urobilin.

While waiting before making the spectroscopic examination the second 10 c.c. portion is tested for bilirubin. To the duodenal contents in the second 25 c.c. graduate is added exactly 10 c.c. of 10 per cent. aqueous solution of calcium chloride made slightly alkaline to litmus with normal sodium hydrate solution. The mixture is thoroughly shaken and then poured into two 15 c.c. centrifuge tubes, 10 c.c. in each. It is then rapidly centrifugalized for a few minutes to collect the precipitate into a compact mass. The supernatant fluid is decanted and the residue washed out of the tubes with a few cubic centimeters of acid alcohol<sup>‡</sup> into a porcelain evaporating dish. In all, about 20 c.c. of acid alcohol is used to dissolve the precipitate. The alcohol mixture is carefully heated on a copper warming stage and allowed to boil vigorously. The color, which may be brick red, soon changes to green if there is much bilirubin present. The mixture is concentrated so that its volume just reaches the "U" in an Esbach albuminometer. Alcohol is added to the mark "R." The color of the fluid by transmitted light is then compared with three standard tubes marked +, + +, + + +,

<sup>\*</sup> Ethylalcohol, 500 c.c.; zinc acetate, quantity sufficient for saturation.

<sup>†</sup> Paradimethylaminobenzaldehyde, 4 gm.; hydrochloric acid, 30 c.c.; distilled water, 30 c.c.

<sup>‡</sup> Hydrochloric acid, 5 c.c.; alcohol, 20 c.c.



according to the shade of emerald green as viewed by transmitted light. The standard tubes are prepared arbitrarily from specimens containing appreciable amounts, moderately large amounts, and excessive amounts of bilirubin. These alcoholic solutions may be kept indefinitely without change of color, though it may be advisable to place the tube in the dark when it is not in use.

The first mixture is now examined spectroscopically for urobilinogen and urobilin. The spectroscope we use is of the simple students' type having a collimator, with a slit adjustable by a thumb screw, a scale tube, and a draw-tube type of telescope. The light we use is a 250-Watt Tungsten electric lamp mounted on a stand with a green shade reflector. This is adjusted so that when the collimator of the spectroscope is placed about eight inches from the globe a brilliant spectrum is produced. The glare of the light is kept from the eyes by the shade of the lamp, and by a shield of black cardboard perforated so that it may be slipped on the collimator tube. For observing the absorption bands, Schneider uses a 50 c.c. graduated cylinder. Our own observations were made in this manner up to October 1, 1916; since that time we have used a spectrum cell with parallel sides, and of such dimensions that the distance traversed by the rays of light in passing through the fluid is exactly 1 cm. Schneider opens the slit of the collimator eight half-turns or four full turns of the adjusting screw when using a cylinder for examining the solution. We have found this slit too wide with the standard spectrum cell, and have accordingly used a slit of just half the width. Thus to adjust the collimator we completely close the slit and then open it by four half-turns or two complete turns of the adjusting screw. This gives apparently about the same degree of absorption with the standard cell as is obtained with the cylinder when the slit is twice as wide, so that in this way all readings are made to conform to Schneider's standard.

The presence of urobilin is marked by a broad band in the blue end of the spectrum. The violet rays are completely absorbed, and if there is much urobilin present the entire blue portion and nearly all of the green may be obliterated. Urobilinogen absorbs a narrow portion of the spectrum in the yellow at the edge of the green, and if present in large amounts the band may be broad enough to obliterate the entire yellow portion of the spectrum. It is located by its proximity to the "D" Fraunhofer line while urobilin extends from between the "B" and "F" lines to the violet end of the visible spectrum.

The method used by Schneider to estimate the quantity of the absorbing substances is that suggested by Wilbur and Addis. The solution is diluted carefully with alcohol until the absorption bands disappear. The urobilinogen and urobilin differ in their intensity; consequently the disappearance of the absorption bands will occur with different dilutions, although at times the same dilution causes

the clearing of the spectrum in both regions. The end-point is determined when the absorption band disappears, but can be made out faintly when the slit is narrowed to just half of its former opening; that is, when the cylinder method is used the adjusting screw is turned four half-turns. With the standard spectrum cell the end-point is determined by causing the reappearance of absorption bands with two half-turns.

The amount of urobilin and urobilinogen is estimated according to the Wilbur and Addis method for 1000 c.c. by multiplying the number of dilutions by 200. This factor is used since 5 c.c. of duodenal contents is represented in 10 c.c. of filtrate obtained from the mixture with the Schlesinger solution. The number of units of urobilinogen and urobilin are added together and the total number of units reported, *e. g.*, urobilinogen (three dilutions)  $3 \times 200 = 600$  units; urobilin (four dilutions)  $4 \times 200 = 800$  units; total 1400 units.

#### CLINICAL OBSERVATIONS.\*

A total of 119 tests have been made in 89 cases. The results will be considered in three groups:

1. Results obtained in a series of miscellaneous cases of which there were 22, and 22 tests.
2. The findings in hemolytic jaundice, 6 cases, 12 tests.
3. The findings in pernicious anemia, 61 cases, 85 tests.

The study includes the tests made in all cases up to November 15, 1916, with the exception of 9 in which the diagnoses were so obscure as to render the results positively and negatively valueless. Brief protocols of the 22 cases in the miscellaneous group are presented.

#### 1. MISCELLANEOUS CASES.

*Anemia from Hemorrhage.* CASE 1 (157200).—Woman, aged fifty years. Uterine myomas. Hysterectomy. Spleen normal in size but hard; liver congested. Hemoglobin, 30 per cent.; red blood cells, 3,470,000.

Duodenal contents: Color, yellow. Urobilin, 200 units; urobilinogen, trace; total, 200+ units.

CASE 2 (164791).—Woman, aged forty-one years. Hysterectomy. Appendectomy. Spleen twice normal size; liver slightly enlarged. Hemoglobin, 35 per cent.; red blood cells, 3,190,000.

Duodenal contents: Color, yellow. Urobilin, 200; urobilinogen, 0; total, 200.

CASE 3 (156514).—Woman, aged forty-seven years. Cervical polyp. Melancholia of climacteric. Liver normal; spleen normal. Hemoglobin, 50 per cent.; red blood cells, 3,600,000.

Duodenal contents: Urobilin, 200; urobilinogen, 0; total, 200.

\* Made by Giffin.

CASE 4 (160583).—Man, aged fifty-nine years. Bleeding hemorrhoids. Liver just palpable; spleen normal. Hemoglobin, 30 per cent.; red blood cells, 3,340,000.

Duodenal contents: Color, yellow. Urobilin, trace; urobilinogen, trace; total less than 200.

CASE 5 (172166).—Woman, aged twenty-five years. Slight menorrhagia. Liver normal; spleen normal. Hemoglobin, 60 per cent.; red blood cells, 4,460,000.

Duodenal contents: Color, yellow. Urobilin, 500; urobilinogen, 0; total, 500.

*Chronic Arthritis.* CASE 6 (85456).—Man, aged fifty-one years. Mild arthritis and neuralgia. Liver normal; spleen just palpable. Hemoglobin, 72 per cent.; red blood cells, 4,620,000.

Duodenal contents: Color, yellow. Bilirubin trace. Urobilin, 800; urobilinogen, 0; total, 800.

CASE 7 (131120).—Man, aged fifty years. Mild chronic arthritis; dental abscesses; chronic tonsillitis. Liver normal; spleen normal. Possibility of pernicious anemia. Hemoglobin, 38 per cent.; red blood cells, 1,700,000; white blood cells, 12,200; color index, 1.1. (One year ago hemoglobin 57 per cent.; red blood cells 4,080,000.)

Duodenal contents: Urobilin, 600; urobilinogen, 600; total, 1200.

*Dental Abscesses; Anemia of Secondary Type.* CASE 8 (162929).—Woman, aged thirty-two years. Liver normal; spleen just palpable. Hemoglobin, 52 per cent.; red blood cells, 4,520,000.

Duodenal contents: Color, yellow. Bilirubin trace. Urobilin, 600; urobilinogen, 0; total, 600.

*Cholelithiasis.* CASE 9 (151433).—Woman, aged fifty-seven years. Gall-stones. Slight possibility of pernicious anemia. Cholecystectomy. Liver normal; spleen normal. Hemoglobin, 49 per cent.; red blood cells, 2,360,000; color index, 1.

Duodenal contents: Color, yellow. Urobilin, 600; urobilinogen, 0; total, 600.

*Syphilis.* CASE 10 (153153).—Woman, aged thirty-two years. Syphilis of the liver and spleen. Splenectomy, April 29, 1916; spleen 760 grams. Liver very large with gummas and contractures. Hemoglobin, 49 per cent.; red blood cells, 3,430,000.

Duodenal contents: Color, yellow. Urobilin, 1000; urobilinogen, trace; total, 1000+.

CASE 11 (151226).—Woman, aged thirty-four years. Probable luetic anemia. Some evidence of nephritis. Absence of history of pernicious anemia. Liver normal; spleen normal. Hemoglobin, 45 per cent.; red blood cells, 3,330,000; color index, 0.6.

Duodenal contents: Color, yellow. Bilirubin, trace. Urobilin, 800; urobilinogen, 0; total, 800.

*Carcinoma.* CASE 12 (169462).—Man, aged forty-five years. Carcinoma of stomach. Roentgen findings of extensive carcinoma. Wassermann negative. Hemoglobin, 29 per cent.; red blood cells, 3,190,000.

Duodenal contents: Color, yellow. Urobilin, 400; urobilinogen, trace; total, 400+.

*Tuberculosis.* CASE 13 (162671).—Woman, aged thirty years. Tuberculous salpingitis. Tuberculous peritonitis found at operation elsewhere. Moderate splenomegaly. Hemoglobin, 35 per cent.; red blood cells, 4,410,000.

Duodenal contents: Color, brown. Bilirubin, ++. Urobilin, 400; urobilinogen, 600; total, 1000.

*Chronic Septic Splenomegaly.* CASE 14 (154572).—Woman, aged thirty-one years. Chronic septic splenomegaly. History of scarlet fever, frequent sore throat and "la grippe." Attacks of left upper abdominal pain two years. Cesarean section fifteen months previously. Two weeks afterward excruciating upper abdominal pain. Exploration elsewhere; large spleen found but nothing done. History suggestive of abdominal thrombophlebitis. Splenectomy April 12, 1916; spleen, 365 grams. Multiple infarcts. Hemoglobin, 50 per cent.; red blood cells, 4,600,000; white blood cells, 10,400.

Duodenal contents: Color, yellow. Urobilin, 400; urobilinogen, 0; total, 400.

*Splenic Anemia.* CASE 15 (158085).—Man, aged twenty-nine years. Splenic anemia. History of severe hemorrhages. Melena. Splenectomy; spleen, 780 (?) grams; liver moderately enlarged. Hemoglobin, 45 per cent.; red blood cells, 3,330,000; white blood cells, 3600.

Duodenal contents before splenectomy: Color, yellow. Bilirubin, trace. Urobilin, 1000; urobilinogen, 200; total, 1200.

*Portal Atrophic Cirrhosis of Liver.* CASE 16 (148570).—Man, aged sixty-two years. Portal atrophic cirrhosis of the liver. History of alcoholism. Ascites. Liver, 720 grams; spleen, 450 grams. Hemoglobin, 70 per cent.; red blood cells, 3,530,000.

Duodenal contents: Color, yellow. Bilirubin, ++. Urobilin, 1000; urobilinogen, trace; total, 1000+.

*Polycythemia.* CASE 17 (174186).—Man, aged fifty-one years. Polycythemia. Cyanosis. Liver moderately enlarged; spleen moderately enlarged. Diabetes, ten-year history. Nine months previously red blood cell count elsewhere, 9,500,000. Roentgen-ray treatment with improvement. At present hemoglobin, 93 per cent.; red blood cells, 5,320,000. Coagulation time ten minutes (Boggs). Bleeding time, five minutes.

Duodenal contents: Color, brown. Bilirubin, +++. Urobilin, 500; urobilinogen, 500; total, 1000.

*Myelogenous Leukemia.* CASE 18 (157746).—Man, aged thirty-two years. Spleen enormously enlarged; liver slightly enlarged. Slight degree of jaundice. Duration of history, one and a half years. Splenomegaly one year. Hemoglobin, 45 per cent.; red blood cells, 3,120,000; white blood cells, 496,000; myelocytes, 43.7 per cent.

Duodenal contents: Color, yellow. Urobilin, trace; urobilinogen, trace; total less than 200.

CASE 19 (158647).—Man, aged fifty-two years. Spleen enormously enlarged. Liver normal. Jaundice questionable. Length of history, one year. Splenomegaly, six months. Hemoglobin, 55 per cent.; red blood cells, 3,450,000; white blood cells, 307,000; myelocytes, 29.7 per cent.

Duodenal contents: Color, yellow. Bilirubin, trace. Urobilin, 2000; urobilinogen, 540; total, 2540.

CASE 20 (159989).—Man, aged thirty-nine years. Spleen moderately enlarged; liver normal. Jaundice? Length of history, twenty-two months. Splenomegaly, ten months. Hemoglobin, 53 per cent.; red blood cells, 3,210,000; white blood cells, 341,000; myelocytes, 29 per cent.

Duodenal contents: Color, yellow. Urobilin, 800; urobilinogen, 0; total, 800.

CASE 21 (173747).—Man, aged thirty-nine years. Spleen enormously enlarged; liver moderately enlarged. Slight jaundice. Splenomegaly, two years. Hemoglobin, 42 per cent.; red blood cells, 2,180,000; white blood cells, 8200; myelocytes, 15.7 per cent.

Duodenal contents: Color, brown. Bilirubin, +++. Urobilin, 900; urobilinogen, 200; total, 1100.

*Combined Sclerosis.* CASE 22 (154069).—Man, aged thirty-eight years. Very ataxic; duration six months. Neurological examination showed findings of advanced combined sclerosis. Wassermann tests negative. Hemoglobin, 54 per cent.; red blood cells, 3,720,000; color index, 0.7. The existence of pernicious anemia is highly probable.

Duodenal contents: Color, brown. Bilirubin, +++. Urobilin, 5500; urobilinogen, 2000; total, 7500.

A summary of the values is given in Table 1.

TABLE 1.—MISCELLANEOUS CASES: SUMMARY OF VALUES.

	Cases.	Urobilin.	Urobilinogen.
Anemia from hemorrhage (averages)	5	275 +	0 or trace
Chronic arthritis (averages)	2	700	300
Dental abscesses	1	600	0
Cholelithiasis	1	600	0
Syphilis (averages)	2	900	0 or trace
Carcinoma	1	400	Trace
Tuberculous salpingitis	1	400	600
Chronic septic splenomegaly	1	400	0
Splenic anemia	1	1000	200
Portal atrophic cirrhosis	1	1000	Trace
Polycythemia	1	500	500
Myelogenous leukemia (averages)	4	925 +	185
Combined sclerosis (pernicious anemia?)	1	5500	2000

All of these patients save 3 suffered from a moderate or severe anemia. The patient with polycythemia had a hemoglobin of 93

per cent. and a red cell count of 5,320,000 at the time of examination; the value for urobilin was 500 units, and that for urobilinogen 500 units. The patient with portal cirrhosis had a hemoglobin of 70 per cent. and a red cell count of 3,530,000; the urobilin was 1000 units and urobilinogen a trace. One of the patients with chronic infectious arthritis had a hemoglobin of 72 per cent. and a red cell count of 4,620,000; the urobilin was 800 units and urobilinogen zero. These three determinations are unaffected by anemia. They all show total values of approximately 1000 units. It has been concluded by other observers that total values of 1000 units or less are normal.

The values in cases of anemia from hemorrhage were especially low, possibly indicating an actual decrease of blood destruction below normal. In anemias of infectious origin, in syphilis, in carcinoma, and in cirrhosis of the liver the total values for urobilin and urobilinogen were 1000 units or less. Three of 4 patients with myelogenous leukemia gave low determinations; in 1, however, the total was 2540 units.

The group, as a whole, demonstrates consistently low values for the purely secondary types of anemia, irrespective of the severity of the anemia. Patients with simple anemia from hemorrhage present the lowest values of the series.

## 2. HEMOLYTIC JAUNDICE.

Twelve determinations of the pigments in the duodenal contents have been made in 6 patients with hemolytic jaundice. Brief protocols of these cases follow:

CASE 1 (112836).—Woman, aged forty-nine years. Acquired type of hemolytic jaundice, with the blood picture of a primary anemia. Increased fragility of erythrocytes. Gall-stones and a large slightly cirrhotic liver were found at operation. Weight of spleen, 910 grams. Patient returned during relapse one year and eight and a half months after splenectomy. The liver was then very large. Hemoglobin, 45 per cent.; red blood cells, 3,260,000; white blood cells, 3400; normoblasts, 152 in 300 cells. Duodenal test one year, eight and a half months after splenectomy: Color, brown. Bilirubin, ++++. Urobilin, 3000; urobilinogen, 1000; total, 4000. The patient improved markedly after two transfusions, but a subsequent estimation of the pigments was not made.

CASE 2 (153245).—Woman, aged thirty-eight years. Severe case of congenital type, with enlarged liver and gall-stones. Increased fragility of erythrocytes. Weight of spleen, 1700 grams. Hemoglobin, 47 per cent.; red blood cells, 2,840,000; white blood cells, 9800; no normoblasts.

Duodenal test one day before splenectomy: Color, yellow. Bilirubin, ++++. Urobilin, 4600; urobilinogen, 1000; total, 5600.

Thirty-eight days after splenectomy: Color, yellow. Bilirubin, trace. Urobilin, 1400; urobilinogen, 1800; total, 3200. The hemoglobin at the time of the latter test was 70 per cent.; red cells, 4,960,000; no normoblasts.

CASE 3 (148209).—Man, aged twenty years. Mild case of congenital type. Increased fragility of erythrocytes. At operation the liver showed evidence of early cirrhosis. Weight of spleen, 300 grams. Hemoglobin, 70 per cent.; red blood cells, 4,920,000.

Duodenal test forty-seven days before splenectomy: Color, yellow. Bilirubin, trace. Urobilin, 1400; urobilinogen, 1000; total, 2400. Fourteen days before splenectomy: Color, yellow. Bilirubin, trace. Urobilin, 2000; urobilinogen, 1200; total, 3200. Thirteen days after splenectomy: Color, yellow. Urobilin, 800; urobilinogen, 1000; total, 1800. One hundred and forty days after operation: Color, yellow. Urobilin, trace; urobilinogen, 400; total, 400+.

CASE 4 (161538).—Woman, aged twenty-seven years. Moderately severe case of congenital type. Increased fragility of erythrocytes. Liver probably normal. Gall-stones present. Weight of spleen, 560 grams. Hemoglobin, 64 per cent.; red blood cells, 3,860,000.

Duodenal test three days before splenectomy: Color, yellow. Urobilin, 500; urobilinogen, 500; total, 1000. Twenty-three days after splenectomy: Color, light brown. Bilirubin, trace. Urobilin, 400; urobilinogen, 0; total, 400. At the time of the latter test the hemoglobin was 70 per cent.; red blood cells, 4,680,000.

CASE 5 (162670).—Man, aged thirty-one years. Moderately severe case, probably of congenital type. Increased fragility of erythrocytes. Liver normal. Gall-stones present. Spleen weighed 1250 grams. Hemoglobin 67 per cent.; red blood cells, 3,650,000. Considerable deformity of red cells.

Duodenal test four days before splenectomy: Color, brown. Bilirubin, ++++. Urobilin, 1400; urobilinogen, 1800; total, 3200. Twenty-one days after splenectomy: Color, brown. Bilirubin, ++. Urobilin, 1000; urobilinogen, 200; total, 1200. The hemoglobin at the time of the latter test was 80 per cent.; red blood cells, 4,022,000.

CASE 6 (153653).—Man, aged twenty-three years. Mild case with some evidence that a familial factor was present. Increased fragility of erythrocytes. Non-operative. Spleen moderately enlarged. Hemoglobin, 60 per cent.; red blood cells, 3,900,000; white blood cells, 5800; no normoblasts.

Duodenal test: Color, dark yellow. Bilirubin, +. Urobilin, 3000; urobilinogen, trace; total, 3000+. (The low urobilinogen may have been due to delay in making the estimation.)

The values for urobilin and urobilinogen in the duodenal contents are very markedly increased in cases of hemolytic jaundice. A few reported cases have shown even higher values than those we have

demonstrated. High values are found even when a moderate degree of anemia is present. In Case 3 at the time of the first two tests the anemia was not severe; however, abnormally large amounts of pigment were obtained. Severe grades of anemia are associated with very high values; in Case 2, with a red count of 2,840,000, the total values were 5600 units. If these values are a reasonably accurate index of hemolysis, blood destruction in hemolytic jaundice is probably much increased at a time when blood production is not seriously affected. This is in contrast to our experience with pernicious anemia in which the evidence of bone-marrow insufficiency is usually marked and the evidence of blood destruction extremely variable. Patients with pernicious anemia who show high values for urobilin and urobilinogen at a time when the blood count is low frequently show very low values when the blood count has risen to the level of a moderate anemia. Patients with hemolytic jaundice, on the other hand, may show high values with only a slight anemia. In 2 patients with very high values the blood picture simulated that of pernicious anemia. An excessive degree of blood destruction probably exhausted the bone marrow.

In 4 of these patients tested before and after operation there was an appreciable reduction in the values for bile pigments following splenectomy. In 2 of them a decided decrease in the amount of urobilinogen was revealed. In Case 3 a former operation for cholecystitis had not reduced the values to normal. The preoperative values of these 4 patients averaged 2050 units for urobilin and 1100 units for urobilinogen, a total of 3150 units. The average postoperative values at periods varying from thirteen days to four months after splenectomy were 800 units for urobilin and 625 units for urobilinogen, a total of 1425.

TABLE 2.—ESTIMATION OF PIGMENTS IN THE DUODENAL CONTENTS.  
HEMOLYTIC JAUNDICE.

Case No.	Time before and after splenectomy.	Color.	Bilirubin, units.	Urobilin, units.	Urobilinogen, units.	Total, units.
1 (112836)	1 year 8½ months after	Brown	+++	3000	1000	4000
2 (153245)	1 day before	....	+++	4600	1000	5600
	38 days after	Yellow	Trace	1400	1800	3200
3 (148209)	47 days before	Yellow	Trace	1400	1000	2400
	14 days before	Yellow	Trace	2000	1200	3200
	13 days after	Yellow	0	800	1000	1800
	140 days after	Yellow	0	Trace	400	400+
4 (161538)	3 days before	Yellow	....	500	500	1000
	23 days after	L. brown	Trace	400	0	400
5 (162670)	4 days before	Brown	+++	1400	1800	3200
	21 days after	Brown	++	1000	200	1200
6 (153653)	Non-operative	D. yellow	+	3000	Trace	3000+
Average values before splenectomy			4 cases	2050	1100	3150
Average values after splenectomy			4 cases	800	675	1475



## 3. PERNICIOUS ANEMIA.

Eighty-five estimations were made in 61 cases of pernicious anemia. In 6 of the cases the tests were done only after splenectomy, thereby reducing the number of medical and preoperative observations from 61 cases to 55 cases. The average of the readings for urobilin in these 55 cases was 1856.5 units and that for urobilinogen 1604.5 units. The average total for urobilin and urobilinogen was therefore 3461 units. This average is approximately four times normal and remarkably close to the figure obtained by Schneider in his recently reported series.

Nine of the 55 patients showed total values less than 1000; in other words, 84 per cent. gave values of 1000 units and over. It is our experience that patients more than fifty-five years of age, and particularly more than sixty years of age, not uncommonly show low values. In these senile types there is frequently evidence of advanced bone-marrow damage with little active hemolysis. Some of these anemias may, in reality, be osteosclerotic in origin, but this distinction is difficult to make clinically.

It is also our experience that as the blood improves in pernicious anemia the duodenal values quickly decline. When the red cells reach 3,500,000 the duodenal values are quite apt to run below 1000 units total. The average in 3 patients with red cell counts above 3,500,000 cells was 433.3 units for urobilin and 466.6 units for urobilinogen, making a total of 899.9 units. Moreover, a few patients who have had repeated tests during treatment have shown this same rapid decline in values when the anemia became of moderate grade. Hemolytic jaundice, on the other hand, gave high values even when the anemia was slight.

It is therefore to be concluded that a certain number of patients with undoubted pernicious anemia do show low total values at certain times. On the other hand, urobilinogen will be present in an appreciable amount. The most noteworthy constant is the presence of an estimable amount of urobilinogen. Urobilinogen was absent in only 1 of the 55 medical and preoperative cases; in 2 others there was a trace; in 52 urobilinogen was present in relatively large amounts; in 24, or nearly one-half of the cases, urobilinogen was present in even larger amounts than urobilin. The presence of large quantities of urobilinogen before splenectomy and its complete absence in at least 75 per cent. of the cases after splenectomy are very striking findings and may have an important significance.

The highest total values were obtained in patients with red cell counts between 2.5 and 3.5 million cells. They were slightly lower in patients with erythrocyte counts between 1.5 and 2.5 million cells and considerably lower in patients with erythrocyte counts below 1.5 million cells. The lowest values were obtained in patients

with counts over 3.5 million cells, but even in these urobilinogen was present in a distinctly abnormal amount. The most active hemolysis seems to occur in the patients with counts between 2.5 and 3.5 million cells, but this may be due to the fact that patients are only rarely seen at the onset of a period of active blood destruction. As a group these latter cases show evidence of very active hemolysis and at the same time evidence of active blood production.

TABLE 3.—ESTIMATION OF PIGMENTS IN THE DUODENAL CONTENTS: VALUES WITH RESPECT TO ERYTHROCYTE COUNT.

PERNICIOUS ANEMIA (MEDICAL AND PREOPERATIVE).

	Number of estimations.	Average urobilin, units.	Average urobilinogen, units.	Total, units.
Erythrocytes 1.5 million and below	11	1496.3	1472.7	2969.0
Erythrocytes 1.5 to 2.5 million .	32	1864.3	1425.0	3589.3
Erythrocytes 2.5 to 3.5 million .	13	2346.1	1653.8	3999.9
Erythrocytes 3.5 million and over	3	433.3	466.6	899.9
HEMOLYTIC JAUNDICE (MEDICAL AND PREOPERATIVE.)				
Erythrocytes 3.5 million and over	4	1650.0	850.0	2500.0

*Age.* The average totals for patients under fifty-five years of age showed very little variation by decades. Over the age of fifty-five years there was a decided drop both in urobilin and urobilinogen. Between the ages of fifty-six and sixty years the totals average 2644.2; over the age of sixty years they average 1600, while under fifty-five years the average totals for decades vary between 3325 and 4238.

TABLE 4.—ESTIMATION OF PIGMENTS IN THE DUODENAL CONTENTS: VALUES WITH RESPECT TO AGE.

PERNICIOUS ANEMIA (MEDICAL AND PREOPERATIVE).

Age of patient.	Number of cases.	Average urobilin, units.	Average urobilinogen, units.	Total, units.
30 years and under .	3	2266.6	1833.3	4099.9
31 to 40 . . .	10	1955.0	1370.0	3325.0
41 to 50 . . .	12	2075.0	1691.6	3766.6
51 to 55 . . .	16	2200.6	2037.5	4238.1
56 to 60 . . .	9	1372.0	1272.2	2644.2
Over 60 years . .	5	660.0	940.0	1600.0

*Size of Spleen.* High values were obtained both in patients with large spleens and in those with small spleens. Lower values were obtained in those with spleens of moderate size, that is, weighing from 200 to 500 gm. The highest urobilinogen values were obtained in patients with spleens of 200 gm. and less. It is impos-

sible to determine the significance of these findings with respect to the size of the spleen. The degree of pathological or of functional damage in the liver may be the important factor. Patients with small spleens have more constantly shown evidence of advanced pathological change in the liver.

TABLE 5.—ESTIMATION OF PIGMENTS IN THE DUODENAL CONTENTS:  
VALUES WITH RESPECT TO WEIGHT OF SPLEEN. .

PERNICIOUS ANEMIA (PREOPERATIVE ESTIMATIONS).

Weight of spleen.	Number of cases.	Average urobilin, units.	Average urobilinogen, units.	Total, units.
200 grams and below . . .	4	3000.0	2000.0	5000.0
200 to 500 grams . . .	12	2342.5	1487.5	3830.0
Over 500 grams . . .	6	3233.3	1433.3	4666.6

VALUES AFTER SPLENECTOMY.

A very striking reduction is observed in the values after splenectomy. A total of 19 patients was examined after splenectomy; 13 both before and after operation. The average of the total values for these 13 patients became reduced from 4492.2 to 1134.6 units. Urobilinogen in 10 of the 13 cases was reduced to zero or a trace. Of the entire group of 19 examined after splenectomy, 13 gave values for urobilinogen of zero or a trace. Three showed urobilinogen over 1000 units after splenectomy, but judging from the clinical history these readings probably became reduced later.

Two patients who had high values for urobilinogen following splenectomy, showed no definite improvement in the anemia. The liver was enlarged in each instance and an exposure of the liver to radium was suggested. The application of 50 mg. of radium over five areas for a total of ten hours was followed by a very marked reduction in the size of the liver, a fall in duodenal values and a prompt improvement in the anemia.

TABLE 6.—ESTIMATION OF PIGMENTS IN THE DUODENAL CONTENTS:  
PREOPERATIVE AND POSTOPERATIVE VALUES.

	Number of cases.	Average urobilin, units.	Average urobilinogen, units.	Total, units.
Pernicious anemia (medical and preoperative) . . . . .	55	1856.5	1604.5	3461.0
Pernicious anemia (preoperative) . . . . .	13	2970.7	1521.5	4492.2
Pernicious anemia (postoperative) . . . . .	13	815.4	319.2	1134.6
Pernicious anemia (postoperative) . . . . .	10 of 13	480.0	0 or trace	480.0+
Hemolytic jaundice (preoperative) . . . . .	4	2050.0	1100.0	3150.0
Hemolytic jaundice (postoperative) . . . . .	4	800.0	675.0	1475.0

TABLE 7.—ESTIMATION OF PIGMENTS IN THE DUODENAL CONTENTS. PERNICIOUS ANEMIA (SPLENECTOMY).

Case No.	Date of splenectomy.	Time before and after splenectomy.	Color.	Bilirubin, units.		Urobilin, units.		Urobilinogen, units.		Total, units.		Red blood cells, millions.	Weight of spleen, grams.
				Before operation.	After operation.	Before operation.	After operation.	Before operation.	After operation.	Before operation.	After operation.		
1 (152922)	Mar. 10, 1916	7 days before	Yellow	++	+	2000	1400	600	0	2600	1400	1.96	150
2 (152671)	15, 1916	21 days before	...	...	...	5000	...	1000	...	6000	...	1.48	508
		13 days before	...	...	...	6000	...	4000	...	10000	...	2.94	
3 (154493)	25, 1916	21 days after	...	+	...	3000	...	2000	0	5000	800	4.40	525
		9 days before	Brown	++	+	3500	200	Trace	0	3500+	200	2.34	450
4 (153395)	29, 1916	17 days after	Yellow	++	+	4000	Trace	2000	Trace	6000	8200	1.89	133
		9 days before	Brown	++	+	...	6800	...	1400	...	3200	2.53	
5 (151290)	April 8, 1916	24 days after	Yellow	...	++	...	1800	2600	1400	5800	1400+	3.14	
		9 days before	Brown	++	+	3200	1400	4600	Trace	10000	200	2.80	270
6 (157146)	20, 1916	4 mos. after	Brown	++	+	5400	200	760	0	1600	...	3.25	111
		3 days before	Brown	...	...	840	...	600	...	1100	...	1.96	410
7 (151021)	May 4, 1916	19 days after	Yellow	...	Trace	500	...	600	...	...	...	2.41	
		5 days before	Yellow	+	...	...	...	...	...	...	400	2.22	
8 (157663)	June 2, 1916	27 days after	Brown	...	+	600	400	800	0	1400	200	3.49	192
		1 mo. before	Yellow	...	+	...	Trace	...	Trace	...	200	1.66	
9 (157290)	5, 1916	14 days before	Yellow	...	+	400	Trace	400	0	800	200	5.20	770
		2 mos. after	Yellow	...	Trace	...	Trace	...	0	...	200	2.72	
10 (161677)	15, 1916	18 days before	Yellow	+	++	800	Trace	200	0	1000	200	3.00	300
		6 days before	Yellow	+	++	...	Trace	...	0	...	...	3.33	
11 (160970)	27, 1916	26 days after	Brown	++	+	2500	Trace	2000	...	4500	2200	4.38	300
		11 days before	Yellow	++	+	600	...	600	...	1200	...	1.51	300
12 (158136)	28, 1916	2 mos. before	Brown	++	+	8000	800	2000	1400	10000	2100	1.94	
		7 days before	Yellow	++	+	...	...	...	...	...	1400	2.35	600
13 (170115)	Oct. 3, 1916	23 days after	Brown	++	+	...	800	...	1300	...	2100	2.65	
		8 days before	Yellow	...	+	...	600	...	800	...	1400	3.14	
		1 mo. after	Brown	...	+	...	...	...	...	...	...		
		2 mos. after	Yellow	...	+	...	...	...	...	...	...		

## TRANSFUSIONS.

Transfusions did not seem to affect the duodenal values. However, estimations were not made the first or second day following transfusion, at which time an increase in the amounts of pigments might be expected. Estimations made five and ten days following transfusion gave no unusual values.

## BILIRUBIN.

An excess of bilirubin was usually present when large amounts of urobilin and urobilinogen were found. This relationship was by no means constant. An excess of bilirubin was not infrequently found with low values for urobilin and urobilinogen, and very small amounts of bilirubin were occasionally found with high values. The amount of bilirubin therefore does not run parallel with the values for urobilin and urobilinogen. These values are probably indicative of some quite different function or impairment of function in pathological conditions.

## SUMMARY.

1. With a few slight modifications of technic we have used the method of Schneider in estimating quantitatively the amounts of urobilinogen and urobilin in the duodenal contents obtained by means of an Einhorn tube. The procedures are simple and can be carried out in any clinical laboratory. The results are comparable with those obtained by the more complicated and time-consuming methods in which stool extracts are used for the estimation of these pigments.

2. In a group of 22 miscellaneous cases, low values were obtained in patients with anemia from hemorrhage, carcinoma, tuberculous peritonitis, syphilis, portal cirrhosis, chronic infectious arthritis, and gall-stones. They were low in 3 of 4 patients with myelocytic leukemia. The amounts of these pigments were especially low in cases of anemia from hemorrhage.

3. In hemolytic jaundice the values were consistently high even when severe anemia was not present. The values fell appreciably after splenectomy, but not as promptly as in pernicious anemia.

4. In pernicious anemia the amounts of urobilin and urobilinogen in the duodenal contents were above normal in 84 per cent. of the cases. The amount of urobilinogen was constantly increased when the anemia was severe. Patients over the age of fifty-five showed lower values than younger patients. The values presented no definite relationship to the size of the spleen. Following splenectomy there was a very definite decrease in the amounts of urobilin and urobilinogen; the decrease in urobilinogen was especially noticeable.

5. The amounts of bilirubin in the duodenal contents did not run constantly parallel to the amounts of urobilin and urobilinogen.

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## PLEURAL EOSINOPHILIA.

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REVIEWING 2758 articles for his monograph on eosinophilia, E. Schwarz,<sup>1</sup> in 1914, was able to find but 68 cases of pleural eosinophilia, although this condition had been described by Widál and Ravaut<sup>2</sup> as early as 1900. Bayne-Jones<sup>3</sup> believes the phenomenon occurs more frequently than this would seem to indicate, and attributes the small number of reported cases to the fact that many pleural fluids have not been examined microscopically and that relatively few have been stained with polychrome dyes. According to Bayne-Jones, pleural eosinophilia occurs in about 1 to 5 per cent. of all cases of pleural effusion, as determined by investigators applying constant methods to cases in series.

In many cases of primary pleurisy, when the fluid is examined on the first day of its appearance, a very slight, transient eosinophilia is noted.<sup>4</sup> This eosinophilia vanishes rapidly before the onrush of the neutrophiles. Again during convalescence, eosinophiles may be encountered in small numbers. In these cases, however, the percentage of eosinophiles seldom reaches and does not exceed 5 per cent., in marked contrast to the so-called group of true pleural eosinophilias where these cells range from 10 per cent. upward, and

<sup>1</sup> Die Lehre von der allgemeinen und örtlichen "Eosinophilie," Erbeg. d. allg. Path. u. path. Anat., 1914, xvii, 138-790.

<sup>2</sup> Applications cliniques de l'étude histologique des epauchements sero-fibrineux de la plèvre, Compt. rend. Soc. de biol., 1900, 648.

<sup>3</sup> Pleural Eosinophilia, Bull. Johns Hopkins Hosp., 1916, xxvii, 12.

<sup>4</sup> Malloizel: Recherches anatomo-cliniques sur les reactions pleurocorticales, Thèse de Paris, 1907.

are, in addition, of rather early appearance and far greater persistence. Bayne-Jones's figures<sup>5</sup> as to incidence probably include the relative as well as the true pleural eosinophilias.

The etiology of pleural eosinophilia is purely a matter of speculation. It has been found in connection with such a varied pathology as to be devoid of diagnostic significance. With the exception of one patient with gonorrheal sepsis<sup>6</sup> in no case has the causal germ been one in whose products of inflammation eosinophilia is ordinarily encountered. Among the other conditions with which it has been found are trauma, tuberculosis, sepsis, typhoid fever, syphilis, pleuropericarditis, pneumonia, polyarthritis, nephritis, pulmonary gangrene, hemorrhagic infarct of the lung, endothelioma, septic endocarditis, myocarditis, cardiac insufficiency, puerperal sepsis, neoplasm, and influenza. In practically all of the cases the effusions have been comparatively small, and most have been sterile.

The local often precedes the general eosinophilia and usually exceeds it in degree. In most instances the local is first to disappear. This has been interpreted by some as pointing to a local production of eosinophiles. Others explain it as follows: The local accumulation of cells occurs in response to the irritation of definite eosinotactic substances, probably protein split products in the exudate undergoing absorption. If their field of action extends to the bone marrow the blood eosinophilia follows. If the irritability of the hematopoietic system persists longer than the local eosinotactic stimulus we find the general outlasting the local eosinophilia.

Attention has been called to the small number of cases associated with tuberculosis, the most frequent cause of pleural effusion. This, however, is not surprising. In tuberculosis the pleural involvement is usually of slow, insidious onset and the absorption of the effusion is correspondingly slow and gradual. In most cases of tuberculosis we find a decrease of the eosinophiles in the blood, this decrease becoming more pronounced as the disease approaches a fatal termination and the patient loses his power of reaction. On the other hand, tuberculin injections have been shown to produce at least transient eosinophilias in cases not too far advanced, and attempts have been made to use this reaction as a guide to treatment. It is probable that in the cases with pleural effusion there are ordinarily not sufficient protein split products liberated to produce an eosinophilic reaction. In addition to this, we must remember that in tuberculosis the pleura is often thickened, adhesions frequently walling off and confining the effusion, and that a thickened pleura or fibrinous deposits naturally offer greater barriers to the absorption of protein split products present in the effusion.

The following case was recently reported by Petzetakis:<sup>7</sup> In the

<sup>5</sup> Bayne-Jones: *Loc cit.*

<sup>6</sup> Jacob, F. H.: A case of Gonococcal Pyemia, *British Med. Jour.*, 1907, xii, 203.

<sup>7</sup> Reactions pleurales parabrônchitiques, *Bull. et mêm. Soc. med. d. hôp. de Paris*, 1916, xl, 1545.

course of an acute bronchitis very slight bilateral effusions were discovered, possibly only because the author was studying so-called "parabronchitic pleural reactions." The right-sided effusion was found on the first day of observation. It contained no eosinophiles. On the third day there were 4 per cent.; on the fifth, 10 per cent.; whereas on the left side there were none. On the seventh day no fluid could be obtained from the left side; the right contained 41 per cent. eosinophiles; seven days later but 15 per cent. The blood showed 1 per cent. on the third day, 1.5 per cent. on the fifth, 2 per cent. on the seventh, and 8 per cent. on the ninth day.

Bayne-Jones has analyzed the 8 cases of eosinophilic pleurisy previously collected by Schwarz and has added 1 case of his own to the list. I have had 2 cases of pleural eosinophilia under observation, presenting rather unusual clinical features.

CASE I.—A. A.; white; aged twenty-nine years; seen at the French Hospital in consultation with Dr. Paul Campiche.

The patient was a cook, born in Switzerland; had been in Alaska; never visited the tropics. He had never been ill before the onset of his present trouble. Six months previously he had been found in perfect health and was admitted to a Swiss Relief Society.

His present illness began with cough, pain in the anterior chest, vomiting, and diarrhea. The symptoms lasted six days before hospital admission.

Physical examination showed a well-developed and well-nourished man, with a temperature of 102°, and a weak, regular, possibly dicrotic pulse. The face was flushed. The patient looked anemic. The area of cardiac dullness was not increased; a loud, systolic murmur was audible in mitral and pulmonic areas. The chest showed a slight fulness at the right base posteriorly, with slight dullness at the right base and right axilla, with bronchial breathing and a few small moist rales. The abdomen was tympanitic, with no tenderness, tumors, or roseola. The liver and spleen were not enlarged.

The temperature chart, in connection with the above symptoms and signs, led to a diagnosis of an initial pneumonia, in which the crisis had taken place and been succeeded by a pleural exudate which possibly had become purulent. The general condition and the history of diarrhea suggested the possibility of typhoid or miliary tuberculosis, though the fever curve was rather that of a septic process. A needle was introduced in the dull area at the right base, but no fluid was obtained. Urine showed albumin and a positive diazo. The white blood cells were 8200, with polynuclear neutrophils, 74 per cent.; lymphocytes, 25 per cent.; large mononuclears, 1 per cent.; no eosinophiles; no plasmodia. One stool consisted of almost pure bright red blood, with no mucus, amebæ, parasites, or eggs. Sputum was watery, with traces of blood; just enough obtained to make one smear; few cocci seen; no tubercle bacilli.



Widal reaction was negative at end of forty minutes, with dilution 1 to 40, and two different cultures.

The bloody stool, the first and only one during the course of the disease, suggested an embolic process, though with the leukopenia and positive diazo; typhoid was not absolutely ruled out until a week later, when the Widal reaction was again found negative in all dilutions and blood culture still showed no growth.

Radiographs taken one week later showed a well-defined shadow at right base, extending upward to the scapular spine, and also a mediastinal shadow. After repeated needle punctures on successive days, on one occasion a little serous fluid was obtained. Smears showed numerous leukocytes; no bacteria; no tubercle bacilli.

Ten days after onset the patient developed a thrombosis of the left popliteal and saphenous veins, and showed evidence of a partial pneumothorax. Blood count now was as follows: Hemoglobin, 50 per cent.; red blood cells, 3,500,000; white blood cells, 8000; polynuclears, 74 per cent.; large mononuclears, 4 per cent.; lymphocytes, 18 per cent.; eosinophiles, 0. Wassermann, blood culture, and von Pirquet were negative.

One month after admission radiographs showed: (1) a definite shadow on right side, from about the level of the spine to the angle of the scapula; (2) a shadow as if the dome of the diaphragm were pushed up; (3) large dilated heart; (4) increased shadow of great vessels. Blood count at this time gave: white blood cells, 7600; polynuclears, 74 per cent.; mononuclears, 6 per cent.; lymphocytes, 19 per cent.; eosinophiles, 1 per cent. Widal negative.

Needle puncture made in scapular line right side, ninth space, yielded a yellowish-green serous fluid, which microscopically showed a large number of white blood cells, no red blood cells. Differential count: Polynuclears, 14 per cent.; large mononuclears, 5 per cent.; lymphocytes, 30 per cent.; eosinophiles, 51 per cent. Apparently the upper focus was primary and the effusion secondary to it.

Four days later complement-fixation reactions for syphilis and echinococcus were negative. White blood cells, 4000; polynuclears, 73 per cent.; mononuclears, 4 per cent.; lymphocytes, 22 per cent.; eosinophiles, 1 per cent.

Recovery was steadily progressive and the patient left the hospital three months after admission.

He was next seen four years later, when examination showed that the right lung moved less than the left, but was within normal limits. There were no abnormalities on percussion or auscultation. The right border of the heart extended 1 cm. to the right of the sternum; left border to midclavicular line; sounds were normal. Patient was much stouter than when last seen. Blood: Hemoglobin, 75 per cent.; red blood cells, 4,800,000; white blood cells, 6400; polynuclear neutrophils, 55 per cent.; lymphocytes, 12 per cent.; polynuclear eosinophiles, 32 per cent.; basophiles, 1 per cent.

CASE II.—F. A.; white; male; aged thirty-seven years (Hosp. No. 10697); admitted to the University of California Hospital on January 26, 1916, in the service of Dr. Herbert C. Moffitt. Born in Portugal; had lived in Brazil, age fourteen to twenty-one, working as a farmer on a coffee plantation; in California, age twenty-one to thirty-seven, working in Isleton, on the Sacramento River, raising asparagus.

Family history, habits, and venereal history were unimportant. He had malaria for one month when sixteen and again for two weeks at thirty-one; cured by quinin. In South America had spells of diarrhea, one or two yearly, lasting from three to seven days; no blood.

*Present Illness.* Was well until January 1, 1916.

January 2 he tried to lift a heavy heap of hay and strained his back.

January 3 began to have four or five thin, watery stools daily, with stringy material but no blood. Diarrhea lasted one week. After cessation of diarrhea he began to have dull, frontal headaches and general malaise. Headaches have persisted, but now has no abdominal pain or diarrhea.

January 20 his hearing became impaired and has steadily grown worse.

January 22 he noticed edema of feet, and this has increased to the present. Feels weak and walks with pain. No vomiting or nausea. For the past five days has had increasing cough, with sputum, and for the past two days has had a pain in the left lower thorax, increased by respiration and cough.

*Examination.* Very sick looking; flushed cheeks; respiration rapid; frequent cough. Herpes labialis. Heart very rapid, but not enlarged; sounds normal, except for very faint systolic, probably functional murmur. Lungs: dulness, with absent fremitus and decreased breathing over the left base, not extending beyond the posterior axillary line. Slight Grocco on right side. Friction rub heard just outside the left nipple. Very tender over lower ribs in left axilla and in left upper quadrant of abdomen, but there is no muscle rigidity. Blood: Hemoglobin, 80 per cent.; red blood cells, 5,280,000; white blood cells, 12,000.

*Diagnosis.* Facies and history would suggest typhoid, but breathing and herpes point to a respiratory infection. There is so much tympany in front, on the left side, and such a marked absence of fremitus in the back, that, despite the moderate mobility of the side and the audible breath sounds, the patient probably has a moderate amount of fluid at the left base.

February 2 blood culture was sterile. Wassermann in serum negative. Exploratory puncture of pleural cavity: Needle inserted in line with angle of scapula in both ninth and tenth spaces, but no fluid obtained. Then inserted in ninth space in paravertebral line

and 50 c.c. of straw-colored, murky fluid withdrawn. Pleuritic fluid: fibrin clot settles out with standing. No organisms seen. Cytology: polymorphonuclears, 93 per cent.; endothelials, 4 per cent. lymphocytes, 3 per cent.; many eosinophiles, 30 to 40 per cent. Cultures made from fluid remained sterile. Urine: acid; heavy trace of albumin; urobilin; several hyaline, few granular casts; moderate red and white cells.

Two days later. Sputum cultures: Gram-negative coccus recovered and a few Gram-positive lanceolate diplococci. Sputum washed in normal salt and injected into peritoneal cavity of white mouse. Mouse died February 5, 1916. Smear from peritoneal cavity showed Gram-positive lanceolate diplococci. No Gram-negative cocci. Widal agglutination test: negative in all dilutions. Tuberculin skin test: very slightly positive to human and bovine. Blood: Hemoglobin, 82 per cent.; red blood cells, 5,300,000; white blood cells, 13,000. Polynuclear neutrophils, 70 per cent.; lymphocytes, 7 per cent.; large mononuclears and transitionals, 6 per cent.; eosinophiles, 16.5 per cent.; basophiles, 0.5 per cent. (350 cells counted). Urine: neutral; trace of albumin; casts as above.

Spinal puncture: needle inserted in the fourth lumbar space. Fluid: clear; drops slowly; no increase of pressure; about 15 c.c. withdrawn. Nonne; no Noguchi; faint haze. Fehling's reduced. Cells: one lymphocyte to cubic millimeter. Wassermann in spinal fluid negative. No trichinae found in centrifugalized sediment of fluid; 10 c.c. blood taken and laked with acetic acid. Specimen centrifugalized and examined for trichinae; none found. Stools showed no parasites or ova.

February 1 patient had a short, hacking cough and brought up from 30 to 60 c.c. of heavily blood-stained sputum. Blood: neutrophils, 64 per cent.; lymphocytes, 10.5 per cent.; large mononuclears and transitionals, 10.5 per cent.; eosinophiles, 14.5 per cent.; basophiles, 0.5 per cent. (300 cells counted).

February 4 fluoroscopic examination showed limitation of motion in left diaphragm, which is 1 cm. higher than the right. Movement of right diaphragm increased. Small, well-defined shadow at the left base, distinct from the heart, shading off gradually into the costal shadow above and not affected by change of position.

February 8 the blood was as follows: Hemoglobin, 90 per cent.; red blood cells, 5,350,000; white blood cells, 10,150; polynuclear neutrophils, 68 per cent.; lymphocytes, 10 per cent.; large mononuclears and transitionals, 10 per cent.; eosinophiles, 10 per cent. (148 cells counted).

February 14 no cough, no sputa, and all pain and distress have gone. Temperature is normal. Lungs have cleared except for a little impaired resonance at bases. Blood: Hemoglobin, 80 per cent.; red blood cells, 5,872,000; white blood cells, 11,800; polynuclear

neutrophiles, 48 per cent.; lymphocytes, 12 per cent.; large mononuclears and transitionals, 20.5 per cent.; eosinophiles, 19 per cent.; basophiles, 0.5 per cent. Discharged well.

Both of these patients had atypical pulmonary infections, followed by pleural effusions. In the first case the blood showed 1 per cent. eosinophiles, the pleural fluid 51 per cent. Four years later, long after the patient's complete recovery, the blood still contained 32 per cent. eosinophiles. In the second case the pleural fluid contained 30 to 40 per cent. eosinophiles, the blood 16 per cent., then 14.5 per cent., 10 per cent., and 19 per cent., three weeks after the first count. In the reported cases the local eosinophilia precedes the general, is usually of a greater degree, and is the first to disappear. In our first case four years after the effusion the blood eosinophilia was 32 per cent., a count remarkable for its degree and long persistence. We have found no case recorded presenting these features.

To Dr. Campiche, who placed his patient in my care from the first, and to Dr. Moffitt for the privilege of reporting Case II, I herewith express my appreciation.

# WAR MEDICINE

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## AMERICAN JOURNAL OF CARE FOR CRIPPLES.

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With the entry of the United States into the War the June number of this magazine inaugurates a policy of systematic consideration of the important and enlarged aspects of the care of the cripple which war entails. These have, of course, long since necessitated attention in Europe. The *American Journal of Care for Cripples* should be well qualified for the work it proposes to do. Octavo in size, with page margins of three and four inches, presumably to allow of large, full-page illustrations, it has probably few rivals among magazines at large in substantial impressiveness. Indeed, in these war days wonder is legitimate whether such unusual margins are justifiable. The journal is in its fourth volume and is, of course, already well known to those interested in its aims under peace conditions. The reason for its review in these columns is the added interest of its enlarged scope.

*The United States and the War Cripple.* By way of introduction the editor says under this caption, in part: "The literature on this

subject (The War Cripples) is scanty and scattered, and much of it is available only in foreign languages. Even then most of the material cannot be found outside of libraries in the largest cities. For these reasons the journal will undertake responsibility for making available to its readers much of the significant and authoritative literature dealing with provision for war cripples. The foreign material will appear in English translation, on the literary form of which little emphasis will be laid. The content and information will be the main object of publication. Original contributions are usually valued to an artificial degree by high-standard publications. In a new subject, such as work for war cripples, however, insistence upon original articles would only cause delay and necessitate omission of much valuable matter. The journal will therefore pass on to its readers useful articles from whatever sources they may be obtained. Its best services can be rendered through this policy. In the material published some information may be duplicated or the same work may be reported from varied points of view. But this is a slight disadvantage, and one which cannot be obviated in reproduction from original sources. On the other hand, the expression of divergent opinions may prove of distinct value. The problems are new and a new science of dealing with the adult cripple is being brought into being. New authorities are springing up to meet the demands of national crisis, and the very stress of the situation is producing exceptional results. But the methods developed and the experience gained will be of lasting advantage to the cripple. The editor hopes to have appear in the columns of the journal during the coming year information requisite to an intelligent consideration of problems concerning the disabled soldier."

If it were necessary to comment on the excellence of such purposes, emphasis could be laid on the inclusion here of foreign material in English translation.

*The Battle Gound for Wounded Men.* In a rather colloquial article, Kellogg presents a most interesting survey of the agencies operative in Canada for the returned crippled. Beginning with the overseas return transportation there is a brief account of the civilian commission under which this is accomplished: "Almost by accident, Canada put into the hands of a civilian commission the handling of this return current of men from overseas. The far-reaching social significance of so doing is only now beginning to lay hold of the public. In testifying before a parliament committee in March the general charged with mustering battalions in Montreal district said tersely that he had no time to consider the handling of returned convalescents—his business was to produce fighting men for the front. Not only do the currents run in opposite directions, but their whole functioning is different. The goal of the Military Hospitals Commission is to take the discards of war and readjust them physically, vocationally, and spiritually to civil life. Gradually as the return current grows in volume, and as the commission becomes better known, its work is being visualized as a great economic and patriotic responsibility and service."

"The Canadian Army Medical Corps had been developed for fifteen years prior to the war. Base and camp hospitals were put in operation to care for the heavy medical work incidental to mustering the expeditionary force. Provision for physical examination of recruits had to be expanded, reorganized and brought to new efficiency following the

rejection of large numbers of unfit men after they had reached England. The corps was constantly drained of some of its most experienced physicians who accompanied the troops overseas. But even had the medical corps been equipped to handle invalided men also, so far as numbers go—and this is a moot point—it is my conviction that the present Canadian system which has vested administrative responsibility for handling returned men in a separate civilian agency is the better one. The physical restoration of a sick or temporarily injured soldier, so that he can return to the ranks, is a job for army doctor and drill master. The rehabilitation of a permanently injured man for the resumption of civilian life where he left off, or even the care of the wide variety of war wrecks who come back from the front, calls into play all manner of specialists, surgeons, psychiatrists, tuberculosis experts, trade teachers, agriculturists and the like.”

The following subjects are then considered in some detail: war consumptives, hospitals for convalescents, vocational work . . . reëducation, “facing life again.” The article makes no pretense at statistical or official statements, and yet by means of individual cases and “human” episodes brings to the fore a tangible picture which a more elaborate treatise might fail to do. There is thus carried an appeal to the social worker at large, the importance of which need not be mentioned.

*The Reëducation and Placement of War Cripples.* This is a ten-page account of largely personal observations concerning the work for crippled soldiers in France. Of all the Allies, this country earliest faced and met the necessity of constructive work on these lines, with the result that today familiarity with her experience and methods is almost fundamental to the best-directed efforts wherever undertaken.

*Report of the Disabled Sailors' and Soldiers' Committee, Local Government Board of Great Britain.* The most interesting feature of this report is the following table, giving figures under date of May 4, 1915:

	Army.	Navy.	Total.
Eyesight cases . . . . .	245	9	254
Wounds and injuries to leg (necessitating amputation) . . .	205	10	215
Wounds and injuries to arm (necessitating amputation) . . .	170	6	176
Wounds and injuries to hand (necessitating amputation) . . .	15	6	21
Wounds and injuries to leg (not necessitating amputation) . . .	277	9	286
Wounds and injuries to arm (not necessitating amputation) . . .	272	3	275
Wounds and injuries to hand (not necessitating amputation of complete hand) . . . . .	224	11	235
Wounds and injuries to head . . . . .	123	4	127
Herniæ . . . . .	96	5	101
Miscellaneous wounds and injuries (not included in above) . . .	129	6	135
Chest complaints (including 200 cases of tubercle of the lungs)	298	4	302
Rheumatism . . . . .	116	6	122
Heart disease . . . . .	284	—	284
Epilepsy . . . . .	47	—	47
Nervous diseases . . . . .	54	11	65
Insanity . . . . .	29	—	29
Deafness . . . . .	134	—	134
Frost-bite . . . . .	6	—	6
Miscellaneous disabilities . . . . .	150	13	163
Total . . . . .	2874	103	2977



*The Royal Orthopedic Reserve Hospital at Nürnberg, Germany.* Under this heading appear three short descriptions of work of rehabilitation in Germany. Although published two years ago (1915) the paucity of data from such sources makes the text worth reading, though there is added nothing not already familiar to workers elsewhere. The articles are rather cursory, with emphasis on certain broadly social details, such as earnings and internal business arrangements. The article concludes with original recommendations, long since adopted in principle and amplified.

*The Problem of the Disabled Soldier.* This article sounds the surest note of any in the current number, and will repay perusal by anyone. With very elemental analysis it considers the precise conditions under which Canada put her forces in the field and proceeds to indicate with a kind of logical synthesis, the general constructive needs to be supplied.

In many respects the principles discussed have closer application to the United States than do analogous principles pertaining to France, England or other countries. Dealing in generalities only the article is one of the most fundamental expositions of the whole problem concerning care of the crippled which have recently come to light and will bear quoting at some length, particularly as some striking paragraphs are nearly complete in themselves and give food for thought.

"It is an interesting commentary upon the nature of the question and upon its importance that the warring nations have adopted measures that are almost identical. Differences in the measures adopted depend not upon any fundamental difference in the principles underlying them but upon differences in the social organization of the nation for which they are designed. Like many other nations, Canada provides an elaborate machinery for removing a man from civil to military life. She is like other nations, also, in that the machinery by which she returns the men of her forces to civilian life is less perfect than that by which they are recruited. The situation should be reversed. The man who joins an armed force is assured a position so long as he remains a soldier or sailor. The man who leaves an army or navy becomes a civilian. At once he is thrown upon his own resources and must commence to gain a livelihood in competition with his fellows; in fairness, no man should be subjected to such hazard until he is fitted to cope with it. This is like no preceding war. It is a war of nations, not of armies. As a result, old methods of providing for ex-soldiers have been found inadequate and new legislation to meet new conditions is being devised and enforced. France and England, for example, are remodeling their laws; Canada which had practically no laws for dealing with ex-soldiers when war commenced, will find it necessary to devise a whole procedure for that purpose. The laws by which France is providing for the return to civilian life of those who have served in her 'armies of the land and sea' are characteristically detailed in their provisions. They are governed in their design by principles similar to those which define the obligation to Canada toward her citizen soldiers and sailors. There is great similarity between these principles and those underlying much of the recent legislation providing compensation for working men injured at their employment. There is sound reason in that similarity. Modern workmen's compensation

laws, such as those of the Province of Ontario, look upon the charge for insuring workmen against unavoidable accident as an item in the cost of producing articles manufactured: about 86 per cent. of the industrial accidents occurring in Germany in 1887 were unavoidable. It follows that the cost of insurance should be added to the price of the article manufactured, and that it should be borne by the consumer; the insurance is a part of the cost of the commodity which he purchases. The manner in which French public opinion on these matters was formed to sound lines is very striking. At first there was a universal tendency to assume that there is nothing left for a disabled man but a lifetime of stagnation as an idle pensioner. A definite policy of public instruction was commenced. In it every method of conveying information was used with all the prestige and authority that official approval could lend. Newspapers, magazines, posters, clergy, trades unions, manufacturers' associations, boards of trade, public service corporations, all united in insisting upon the dual obligation existing between the State and its citizens: there is an obligation upon the State to ensure an independent position to those who have been disabled in its service; and there is an obligation upon the citizen, both to be self-supporting in the measure of the ability remaining to him and to receive from his fellow-citizens no more than is his due. It is much less usual now for a disabled soldier to refuse the treatment by which his disability might be lessened or for him to decline the vocational training by which he might be made self-supporting. All Canadians, soldiers and others, should understand that disabled men who refuse to take advantage of the opportunities for treatment and for training offered to them do so at grave cost to themselves. A man who unreasonably refuses to accept the treatment and training made desirable by his disability penalizes himself; by his own choice he remains less capable of supporting himself than he might be. Moreover, such a man cannot expect to be pensioned for the entire disability existing in him; but only for that portion of the disability which would exist were he to accept reasonable treatment. In France, indeed, it is anticipated by many that the acceptance of appropriate treatment and of appropriate vocational training will be made a military necessity for disabled men. The inadequacy of our educational system becomes very apparent when a full-grown Canadian, a returned soldier, about to leave a hospital cured of a transient disablement, begs to be retained for a little longer in order that his primary education may be completed. If it is done for the disabled soldier, since the lack of education was in nowise dependent upon his military service, a means of obtaining knowledge should exist for every citizen who desires it. A civilian suffering from tuberculosis is permitted, restrained by nothing but the degree of his incapacity, to circulate among his fellows, often to his own detriment and to the danger of those among whom he moves. Can advantage be taken of the peculiar situation of soldiers or sailors suffering from tuberculosis to place restrictions upon them—for the benefit of themselves and their fellows—which are not placed upon civilians? It should be done for soldiers; it is but one of the things which should be done for us all under the authority of a not-yet-established Federal Department of Public Health. If these and similar hardships, unconnected with military service, affecting disabled men, be dealt with

adequately, the first step will have been taken toward remedying some of those defects in our national organization which stress of war has made very plain."

*War Cripples in Austria and Germany.* This is a superficial but interesting survey of the efforts of the chief Central Powers toward rehabilitation of the crippled. It emphasizes, among other things, the enormous losses in the Central Army and the fact that in Austria as well as in Germany the authorities do their utmost to keep cripples out of sight in populated centers. It mentions the "Cripples' Town" outside of Vienna where, in November, 1915, there were nearly 4000 maimed soldiers in more or less permanent residence.

"Supposing an unfortunate man, both of whose legs had been amputated, to arrive in 'Cripples' Town,' it is found by experience that, by the fact of his being with so many others, all of whom are afflicted with the loss of one or more limbs, he is encouraged to try to make the best of his infirmities. In some cases maimed men are actually employed to teach others, showing them what it is possible for a cripple to do, with determination, courage and taking pains. A man with both legs amputated, for instance, is given stumps, and then with the help of a moving rope fastened to a roller he gradually learns to walk again along the hospital passages. When he has learned to walk quite quickly on the low artificial legs he is given higher ones, and so higher and higher until he reaches his natural height once more. The next stage in his training is to learn to use artificial legs with movable knee-joints, so that he can sit and kneel down. Finally, he receives artificial legs, with not only movable knee-joints but also ankle-joints provided with strong springs, so that his gait acquires elasticity. Thus equipped he practises walking about in the hospital garden with no other help than that of a light cane. It is not enough, however, for these crippled soldiers to learn to walk again, or even to dance. They must learn to become once more useful members of society. Consequently, they enter one of the thirty-two workshops in 'Cripples' Town,' where they are put to do the work for which they are best fitted. A man who was a carpenter, for example, but who has a stiff elbow, is set to do planing as the speediest way of recovering the elasticity of the elbow. A locksmith is put to use a file; a man with a stiff shoulder must try to use a saw, and a stiff-fingered man to weave baskets. In Germany and Austria, however, this is becoming a veritable art, and the artificial limbs of before the war are now wholly out of date, to such pitch of perfection have those of today been brought." R. P.

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**Bone-graft Surgery: Its Application to Fracture Caused by Modern Projectiles.**—DOWNER (*Military Surgeon*, September, 1917) gives clinical experiences from Serbia and Russia. The most perplexing problems encountered by the military surgeon are the compound comminuted fractures when there is loss of bone substance. These necessitate the transplantation of living bone to act as an internal fixation splint and to stimulate the formation of new bone. In modelling the bone-graft into wedges and pins and inlays, and in fashioning groove joints and dovetail joints the surgeon needs to have had, in advance, good mechani-

cal training in working with tools. The electric current is available nearly everywhere, not only in towns and cities, but also with the armies. This makes it possible to use motor-driven bone surgery outfits which increase the skill and accuracy of the surgeon. A good motor outfit and a strong extension apparatus are indispensable to the bone surgeon at the front. At the beginning of the war amputations were performed almost indiscriminately upon all the fronts. Later, during the second year of the war, more conservative treatment was used, and there was a great decrease in the number of amputations. Many cases, however, were treated too conservatively. Thus badly shattered legs were placed at once in plaster casts, no attempt being made at drainage, and the wounds of entrance and exit being left as they were found upon the battlefield. Often such casts were left on for six weeks, and when removed great destruction of tissues was found and the casts were full of pus. The writer finds that the conservative treatment is still being overdone. The result of these methods he sees in many of the cases which he has operated on. There had been no incision, no drainage, except that made by the projectile, and the parts had been immobilized by some external fixation appliance. The wounds had been allowed to suppurate, through which a small amount of pus was steadily oozing. Upon opening such wounds there were found many fragments of dead and diseased bone, surrounded by much dense fibrous tissue, resulting from the chronic inflammation. Not only were the fragments dead, but also the fractured ends of the bones had begun to soften, and that there was very little callus formation. Very few cases of comminuted compound fractures treated in this way turn out successfully. The writer thinks it preferable to remove all sequestra at the start, leaving a free drainage, then the application of a plaster cast, with a window cut in, and the wound dressed daily through the window. When all suppuration has ceased a bone-graft should be taken, usually from the tibia, and inserted by the inlay method. With the electrically-driven outfit a suitable graft can be secured in ten to fifteen minutes, and then fashioned very quickly to fit the place for which it is intended. The writer has seen evidence for both the views which are advanced as to the role of the graft. In some cases it has acted merely as a scaffold, all the new bone coming from the host. In one case, however, in which the graft was fractured the fractured ends reunited without the aid of outside tissue, so that it may safely be said that the graft acts as a stimulant, and even when placed in infected areas it causes the formation of new healthy bone. It is much better than a metal plate in many cases, for this has been found to inhibit the formation of bone callus. In performing the operation it is well to use two separate groups of instruments, one for making ready the diseased area and the other for preparing the graft. The plaster casts are left on for four or five months, being changed about once a month. After the removal of the cast, massage and usual post-fracture treatment is begun. The results are so good that so long as there is any healthy host bone left in a limb one is justified in giving bone transplantation a trial.

**Triple Typhoid Vaccine** (*Bacillus Typhosus*, *B. Paratyphosus* A, and *B. Paratyphosus* B).—CRAIG (*Jour. Am. Med. Assn.*, September 22, 1917, lxi, No. 12, p. 1000) states that the necessity for protecting our overseas troops against the paratyphoid fevers has rendered inoculations against *B. typhosus* A and *B. typhosus* B imperative, and the fact that these infections occur also in our own country, and will undoubtedly appear sooner or later in our large cantonments, made it advisable that the entire army should be inoculated as a prophylactic measure. A triple vaccine is prepared at the Army Medical School, Washington, D. C., which contains 1,000,000,000 typhoid bacilli, 750,000,000 paratyphoid A bacilli, and 750,000,000 paratyphoid B bacilli per cubic centimeter. The first dose is 0.5 c.c. and the second and third each 1 c.c. The inoculations are made subcutaneously and at intervals of seven days. Craig concludes, as a result of his studies, that the triple typhoid vaccine, which is the vaccine now adopted for immunizing our entire army against typhoid and paratyphoid fevers, gives as good results in immunization, so far as can be judged by agglutinin curves, as does the typhoid vaccine alone, and that neither the general nor the local reactions following its injection are different in any degrees from those occurring after the inoculation of simple typhoid vaccine. The results, both from a practical and from a theoretical point of view, are all in favor of combining the three organisms in a single vaccine, and it is believed amply justify the use of the triple typhoid vaccine in immunizing our troops against typhoid and paratyphoid fevers. J. M. McC.

**The Relation of Psychology to Military Activities.**—YERKES (*Mental Hygiene*, July, 1917) suggests briefly a few of the varied lines of service in which the psychologists may be of value in the conduct of the war. In recruiting they have an important special task, namely, of classifying men according to their mental characteristics and of indicating their degree of adequacy for military training or special work in the military organization. Current methods of mental examining are unsuited to military demands, and consequently new and specially adapted methods must be prepared if the results are to be trustworthy and practically serviceable. In examining recruits it is their prospective function to help eliminate those who cannot render service worthy of their hire; to ascertain various degrees and kinds of special ability so that the individual shall be placed in a position of maximum usefulness; and to detect those who by reason of mental instability or psychopathic condition demand the attention of the medical expert. Already experimental psychological studies, by means of appropriate measurements, are being made on men being trained in naval gunnery and on men receiving preparatory training in aviation. By means of such studies it is believed that information will be derived which will be of value in selecting men suitable for these services and in discovering individuals who will improve most satisfactorily under training. W. H. F. A.

## REVIEWS

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THE MEDICAL CLINICS OF NORTH AMERICA. Philadelphia Number, Vol. I, No. 2. Pp. 195 to 464. Philadelphia and London: W. B. Saunders Company, 1917.

THIS number presents clinics from the University of Pennsylvania, the Jefferson, the Pennsylvania, the Philadelphia General and the Polyelinie Hospitals of Philadelphia. Among its contributors are twelve internists, a roentgenologist, a serologist, a neurologist and a dermatologist. Some of their articles consist of true bedside clinics, such as are daily given to medical students. Others are more formal presentations of cases, with extensive reference to the literature, and still others are not clinics at all but contributions of a more general nature without any reference to individual patients. The latter are represented by Dr. T. H. Weisenburg's article on poliomyelitis and Dr. John A. Kolmer's article on the diagnostic value of examinations of the cerebrospinal fluid.

Dr. Thomas McCrae, in the opening chapter, analyzes 3 cases of aortitis, placing emphasis upon the rheumatic as well as the luetic etiology. In Dr. Alfred Stengel's contribution is given a workable classification of the nephritides based upon the newer knowledge of these conditions, but emphasizing the clinical rather than the laboratory diagnostic features. Dr. Hobart Amory Hare discusses the indications, and particularly the contra-indications, to the use of digitalis in heart disease. Aortic aneurysm and myelogenous leukemia are illustrated by patients from the clinic of Dr. Joseph Sailer. Dr. David Riesman makes use of the unusual opportunities of the Philadelphia General Hospital in presenting a case of progressive myocarditis. Dr. Henry K. Panoast discusses in his usual conservative manner the value of the roentgen rays as a diagnostic aid in pulmonary tuberculosis and calls attention to the similarity of the fibrosis of this disease to that produced by excessive dust inhalation. Angina pectoris and its allied conditions are presented by Dr. A. A. Stevens. A somewhat exhaustive clinic upon the cardiac arrhythmias is given by Dr. Ross V. Patterson, while Dr. John H. Musser, Jr., describes an interesting case of auricular fibrillation of long duration. Gastric infection and ulcerative endocarditis are treated by Dr. Martin Rehfuess and Dr. Judson Daland respectively. Dr. O. H. Perry Pepper discusses the essentials and limitations of an

average diet. A chapter by Dr. Jay Frank Schamberg upon the causes of reaction after salvarsan should be read by all who use it or allied preparations. Dr. Elmer H. Funk concludes the number with an interesting case of osteitis deformans. T. G. M.

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ANNUAL REPORT OF THE SURGEON-GENERAL OF THE PUBLIC HEALTH  
SERVICE OF THE UNITED STATES FOR THE FISCAL YEAR, 1916.

THESE reports speak for themselves always and necessarily do not permit of detailed description. In this report the pellagra and plague surveys are particularly interesting, however. The problem of vocational diseases and industrial hygiene are considered, but only a beginning has been made in this work. It is interesting to note in the report of studies of child labor problems in Massachusetts in relation to health that diseases and defects of a more serious character are less common among minor cotton-mill employees than in the general school population of the same ages.

The present volume contains reports on (1) scientific research; (2) foreign and insular quarantine and immigration (maritime quarantine); (3) domestic (interstate) quarantine; (4) sanitary reports and statistics; (5) marine hospitals and relief; (6) personnel and accounts; (7) miscellaneous. C. W. S.

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THE PRINCIPLES OF ACIDOSIS AND CLINICAL METHODS FOR ITS STUDY. By ANDREW WATSON SELLARDS, Associate in Harvard Medical School Department of Tropical Medicine. Pp. 117. Cambridge-Harvard University Press, 1917.

THIS book is essentially an analysis of the more important and representative articles on acidosis, and is a most excellent presentation of the subject. Clear and succinct in detail, and with a positiveness in deduction, it is very readable and leads through the bewildering chaos of the literature in a no uncertain manner so far as our present knowledge permits. The places where our information is still incomplete are pointed out with equal detail.

Following a short historical note he reviews the equilibrium between acids and bases and the methods of diagnosing acidosis. The determination of the tolerance to sodium bicarbonate he maintains is the most delicate test we have of acidosis, but presents fully the relative value of the various tests with their respective techniques.

Regarding the definition of acidosis, he deprecates the confusing subdivisions and broadly defines the term as a depletion of the

blood and other tissues of the body in fixed bases. Three conditions are known in which severe acidosis occurs, namely, diabetes, some of the nephropathies and the so-called "food intoxication" of children, and these he described fully. He refers but little to the role acidosis may play in the untoward symptoms following general anesthesia. However, his opportunities for studying acidosis in Asiatic cholera while in Manila permit interesting observations which open up new problems. The therapy of acidosis and the technic of sterilizing solutions of sodium bicarbonate are described fully.

C. W. S.

ELEMENTS OF HYGIENE AND PUBLIC HEALTH. A TEXT-BOOK FOR STUDENTS AND PRACTITIONERS OF MEDICINE. By CHARLES PORTER, Medical Officer of Health, London. Pp. 384. New York: Oxford University Press, 1917.

WRITTEN in a most interesting style common to so many of the English writers, this book will be welcomed not only by physicians, but also by all others who are interested in public health. All through the book special emphasis is laid upon the role the practicing physician should assume in community health problems. Too little stress has been made of this point heretofore, the effort having been made more to organize official medical bureaus. As an incentive to secure the coöperation of family physicians, mention is made of the custom in London of paying small fees by the city for the report of communicable diseases.

The first chapter of the book deals with personal hygiene, and is an excellent presentation of the subject, with the possible criticism of his advice to sweeten the water given to infants between feedings, an excellent presentation of the subject, with the possible criticism of his advice to sweeten the water given to infants between feedings, a practice not approved by pediatricians in this country. Then follow several chapters on public health and disease, tropical diseases and animal parasites. A chapter on occupational diseases is of particular interest to physicians of this country at this time, for we are beginning to concern ourselves more and more with this problem. The section on food is excellent. It concerns itself principally with the detection of food poisonous to man and the nature of such poisoning. The chapter on climate and meteorology, however, is elementary, and it is difficult to see the necessity of incorporating such detail in a work of this kind. The air, the soil, water, housing and ventilation, the disposal of refuse and waste are adequately considered in separate chapters.

The book ends with a clear review of the method of computing vital statistics and pitfalls to avoid in interpreting such statistics. An appendix includes copies of leaflets and cards for distribution concerning the care of the baby and contagious diseases.

C. W. S.



PAPERS ON THE INFLUENCE OF SMOKE ON HEALTH. Edited by OSKAR KLOTZ, M.D., and WILLIAM CHARLES WHITE, M.D., Mellon Institute of Industrial Research and School of Specific Industries. Bulletin No. 9, University of Pittsburgh.

THIS bulletin contains the work done by the physicians and laboratory investigators on the staff of the smoke investigation committee of the Mellon Institute of Industrial Research.

Dr. Cohoe's paper on the "Relation of Atmospheric Smoke and Health" gives a review of the literature on the subject, with the vital statistics of communities noted for their smoke. He wisely does not attempt any definite conclusion from a statistical study, but shows unmistakably the marked influence of the smoke in raising the death-rate in acute lung diseases.

Dr. Oskar Klotz's paper on "Pulmonary Anthracosis" is a complete pathological study. The work of Doctors Holman and Haythorn are valuable contributions containing results of original research. Dr. Holman, studying the bacteriology of soot, concludes that soot has some germicidal action, but also as it occurs in smoke, clouds, fogs, etc., protects microorganisms from the destructive action of the sunlight. Dr. Haythorn's study of histological evidences is worthy of particular attention. He concludes that in tuberclosis an anthracotic condition may actively assist healing, in that it is an additional stimulus to fibrosis; but in acute inflammatory conditions an anthracotic condition becomes seriously detrimental because of the *obliteration of the lymphatic spaces*.

The papers make up an exhaustive study, and any future investigation must take cognizance of this work. C. W. S.

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INDEX OF DIFFERENTIAL DIAGNOSIS. By HERBERT FRENCH, M.A., M.D. (Oxon.), F.R.C.P. (Lond.). Second edition. Pp. 911; 37 colored plates and over 300 illustrations in the text. New York: William Wood & Company, 1917.

THE purpose of this book is clearly stated in its title, and the work must be estimated and used in accordance with its expressed purpose. It is an index of differential diagnosis and nothing more. To the question as to whether there is an excuse or need for such an index the repeated printings of the first edition and now the appearance of an enlarged second edition would seem to give sufficient answer.

It is a large book and profusely illustrated with well-chosen and extremely well-reproduced plates, drawings and charts. The many photographs are especially clear and the reproduction of colored photographs are admirable. Apparently nothing is omitted, as

might be suggested by a closely printed index covering almost forty pages, with four columns to the page.

In a month's use as a reference book no serious errors have been found, and except for the very frequent error of putting an umlaut over Prof. Duhring's name on page 219 and a misprint in the page number in the indexing of *Trichina*, no typographical errors were observed.

O. H. P. P.

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OBSTETRICS FOR NURSES. By CHARLES B. REED, M.D., Obstetrician to Wesley Memorial Hospital, Chicago. Pp. 374; 130 illustrations. St. Louis: C. V. Mosby Company, 1917.

THIS book is a practical manual of obstetrics for nurses. The subject is taken up in the following order: A small amount of space is given to anatomy and physiology, followed by normal pregnancy, abnormal pregnancy, labor, the care of the patient during labor and puerperium, operations, complications, infection, the care of the child, infant feeding, a list of diets, solutions and therapeutic index, and a glossary. The book contains good illustrations. The fetal circulation, which many authors fail to give, is described so clearly that any nurse may understand. Dr. Reed endorses the use of nitrous oxide gas in the first part of the second stage of labor, but advises ether or chloroform for the completion of the second stage. The section on the care of the child does not compare favorably with the rest of the book. The care of the premature infant might have been described more fully. The book will be found of practical value for those for whom it is intended.

S. B. S.

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DISEASES OF THE SKIN. By RICHARD T. SUTTON, M.D., Professor of Diseases of the Skin, University of Kansas, School of Medicine, etc. Second edition. Pp. 1021; 833 illustrations. St. Louis: C. V. Mosby Company, 1917.

THIS volume is a large, well-made book. The reviewer not having the privilege of reading the first edition has no means of comparing it with the later edition, but must rely entirely upon his perusal of the volume at hand for his comment. Unfortunately, by reason of his close personal contact with the work and works of Duhring, Stelwagon, Hartzell, Van Harlingen, and Schamberg, representing the so-called Philadelphia school of dermatology, he is too likely to criticize this book unduly severely. In a word, while it is large in size and most formidable in appearance, it may be said not to measure up well to these standard works, although it seems to have been the aim of the author to do so. Pictures, and this term is used advisedly, should make up a large part of any book on dermatology,

but they should be good ones. Here we find the conventional anatomical diagrams, as usual, very good—the photomicrographs or the microphotographs, as the case may be, rather vague in their demonstrating features—and the colored plates of rather indifferent value. The pictures intended to illustrate diseases are very profuse in number but poor in quality, and thereby lose their instructive value. There is also a great abundance of references, but where an author is referred to, there is no means of knowing just what point in the discussion of the disease is attributed to that particular author. Using authorities in that manner renders the value of the bibliography questionable. Here and there throughout the sections on treatment we note obsolete forms of prescription writing. Any formula which has petrolatum for a base, for instance, does not require lengthy Latin or near-Latin instructions to make an ointment out of the ingredients named. It looks imposing but it is unnecessary. The introductory material is especially well handled, that is to say, the anatomy and physiology of the skin and the general etiology and pathology of skin diseases. Usually these chapters in works of this character are awful “bores” and contain all the fables and traditions from Hali Abbas down. Sutton is to be congratulated on his frank denial of “diathesis” and his acceptance and elaboration of occupation as a factor of prime importance in etiology. The relation of proteid substances, toxins and antitoxins to the causation of skin diseases is ably handled. Grouping of the primary lesions as to regional distribution for diagnostic purposes seems unnecessary, however, even if not inaccurate. To our mind and eye, any of the primary lesions not only may but do occur everywhere where the skin is. While this section is rather elaborate, opportunity was neglected to observe the diagnostic significance of pustules in the palms of the hand, on the female breast and on the shaft of the penis in scabies, and the pronounced distribution of the lesions in the different forms of pediculosis. Under general consideration of treatment, Sutton remarks that “purely local cutaneous maladies are indeed few and far between,” with considerable emphasis, as though this were the most modern thought in this field. He qualifies this later by the statement that “constitutional treatment is intended more for the purpose of increasing the bodily resistance of the patient than for any direct or specific effect it may have on the causative factor.” The relation between the general health and skin diseases is always a troublesome topic to handle, since just as we have the matter conclusively proved something embarrassing happens. We refer in passing to the everlasting enigma “psoriasis,” to awaken reminiscences in the reader’s mind. Looking over the book, as a whole, it may be said to include all the legends and mythology of dermatology with the modern frills of treatment, and countless illustrations of indifferent value appended. S. H. B.

# PROGRESS OF MEDICAL SCIENCE

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## SURGERY

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UNDER THE CHARGE OF

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**Wound Treatment.**—DONALDSON and JOYCE (*Lancet*, ii, 1917, 445) say that three main methods of wound treatment are in vogue, the antiseptic, the physiological and the surgical, namely, by excision of the wound. The last named has come into vogue because of the disappointing results obtained from the first two, on the score of their inefficiency or because of the time element. From the physiological or hypertonic saline method has evolved as an outshoot the salt-pack treatment of wounds, for which its advocates claim extraordinarily good results. These include the simplicity of method, the avoidance of daily dressings of the patient, the rapidity with which the wound becomes a healthy granulating surface, the absence of secondary hemorrhage, and the rapid general improvement of the patient. All this means a considerable curtailment of the time spent by the wounded man in hospital. Hitherto the good results have been attributed in some obscure way to the presence of the salt acting more or less on the physiological line described by Wright, but it is felt by all who have written about salt-packs that some other explanation is necessary. Donaldson and Joyce afford what they believe to be the true explanation of the phenomena observed, and believe that it will clear up many of the points that have hitherto been obscure. The key to the situation depends on two observations—one clinical and the other bacteriological. The former consists in the fact that cases which smell (and the odor is one of the most characteristic features of these cases) do well, while those which do not make no headway. The bacteriological observation consists in the discovery that a certain bacillus is apparently constant in the wounds which emit the odor, while it is absent or cannot be recovered from those which do not smell. The bacillus is a spore-bearing anaërobe of a saprophytic nature and belongs to the proteolytic group of organisms, the group which includes *B. tetani* and *B. edematosus maligni*. Unlike these

latter it appears to be non-pathogenic to the animals experimented on, and, what is of more importance, appears to be non-pathogenic for man when introduced into wounds. Further, unlike the above-named pathogenic varieties it does not appear to set free any toxins injurious to the patient in the course of its action on the dead tissues. It acts, apparently, in virtue of its proteolytic powers, only on devitalized tissues, and possibly on toxalbumins, and appears to possess no power of attacking healthy structures. The surgical or excision treatment of wounds aims at removing only microscopically devitalized tissues, and in so doing inflicts a fresh trauma liable to reinfection. It is proposed here to substitute this, the Reading bacillus in a living form, and it is probably present in most of the wounds if given a chance to carry out its functions. These are directed toward the removal not only of the grossly damaged tissue, but it succeeds also in attacking the microscopically damaged structures. As a result the body forces are freed from the constant menace of septic poisoning, thus allowing them to begin the process of repair. Examples are given of gunshot wounds cases which have been treated in various ways previously, but without success. These, however, on being sowed later with living cultures of the bacillus have immediately started to do well and have ended in rapid recovery. The organism is probably present in the large number of infected wounds, but requires more or less anaërobic conditions before it can come into play. It is essential that the wound be thoroughly well laid open in the first instance, exposing every pocket and sinus, so that the packing may completely fill the wound.

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**The Handling of Early and Doubtful Cases of Cancer.**—GREENOUGH (*Ann. Surg.*, 1917, lxvi, 385), basing his conclusions upon the answers to a circular letter to a large number of representative members of the profession, says that the opposition to the use of the exploratory incision for the removal of tissue suspected of malignancy is very real. Many surgeons believe it is never necessary or advisable; others, and they are the majority, believe that in certain situations it is permissible when all other resources of diagnosis (in which should be counted the benefits of consultation) have been exhausted, and even then only (1) when the tumor is a superficial one, or (2) when a frozen section can be obtained immediately and the operation completed under one anesthesia. Under these conditions, and under these conditions only, can the exploratory incision of the tumor tissue be justified as a reasonable surgical procedure. If exploratory removal of tissue is to be discountenanced, what becomes of the project of the free diagnosis of suspected cancer tissue? Greenough believes it assumes an importance greater than ever, because it should be applied to all pathological tissues removed for the cure of disease. The function should be a State function, and the report should go to the patient or his friends as well as to the surgeon. It should be the final means of checking up the end-results of the surgical diagnosis and treatment of malignant disease. Only by some such drastic measures as this can the incompetent surgeon be prevented from depriving the patient of his only hope of cure of cancer by an early operation. In general, superficial and ulcerated lesions are the only ones in which fragments of tissue

may be safely removed for microscopic diagnosis. In deep tumors, where the exploratory incision necessarily opens up normal tissue to infection, exploratory excision of suspected tissue is to be condemned, and should be avoided. Where other resources of diagnosis have been exhausted, and an exploratory incision, with an immediate frozen section diagnosis, and immediate performance of the radical operation if it prove necessary, is the least dangerous procedure for the patient. No suspected tissue should be excised for diagnosis, unless by a surgeon who is equipped to perform immediately the radical operation for the cure of cancer of the organ involved. The routine pathological examination of all tumor tissues removed by operation should be made compulsory. To this end competent laboratories for the free diagnosis of pathological material should be maintained as a function of the State.

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**Posture in Cases of Abdominal Drainage.**—HILL (*Ann. Surg.*, 1917, lxvi, 414) says that abdominal drainage with the patient in the prone position has been tried out at the St. Louis City Hospital so successfully that a number of the staff now use it as a matter of routine. As it is now carried out the patient is placed on the abdomen usually for from twenty-four to forty-eight hours, with the head of the bed elevated about ten to twelve inches. A pillow is placed under the lower part of the chest and one is placed under the head, so as to give the patient ample room to breathe. The principal objection to this position is that it is not comfortable. Their observations lead them to believe, however, that it is not nearly as uncomfortable as one would suppose. By this position are obtained the maximum effects of gravity, intra-abdominal pressure, and capillary attraction. In addition to this there are no spaces in the front of the abdomen to favor the formation of pockets, as there are in the pelvis and alongside of the spine. The pus is also brought against a part of the abdomen where bloodvessels and lymphatics are not nearly so numerous as they are in the pelvis. The lateral position, in which the patient has been placed on the right side, has been found to be very efficient. The head of the bed is slightly elevated, and a pillow is placed under the region of the liver, so as to prevent any space for accumulation of fluid in the kidney region. The patient is placed far enough over so that pus will drain from in front of the left kidney. In an analysis of 104 drainage cases operated on in this hospital during the last year and a half the three positions have been employed with sufficient frequency to warrant drawing some conclusion as to the relative merits of each. In a series of 15 cases of appendicitis of various grades of severity treated in the lateral position there was an absence of mortality. In another series of 42 cases of appendicitis treated in the abdominal position there were but two deaths. In the 47 cases of the same condition treated in the Fowler position there were five deaths.

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**Ultimate Results Following Nephropexy in Cases of Symptomatic Nephroptosis.**—CLARK and BLOCK (*Ann. Surg.*, lxvi, 479) present a study of 50 cases of nephroptosis operated on since 1900. They show a steady diminution in the percentage of elective cases. If one adheres to the rule that surgical intervention is indicated only when the kidney or the bladder gives expression to symptoms the ratio of cure

will compare favorably with that following other approved operative measures. They have settled upon three cardinal indications for possible surgical intervention in movable or floating kidneys. These are fixed pain in the renal area, Dietl's crisis, and marked vesical distress referred from the renal area. Even these symptoms, however clear, must be supplemented and confirmed by a rigid clinical investigation, which should include a cystoscopic examination, catheterization of the ureter on the affected side, and, in the majority of cases, an injection of thorium and a roentgen-ray examination to ascertain the degree of dilatation of the renal pelvis. An appended table of cases operated upon since 1910, the period during which they have endeavored to select only those of a true pathological nephroptosis, with a summary of symptoms, with diagnosis, operation, and ultimate results, present a 70 per cent. restoration to active efficiency of the women operated on, a degree of restoration which compares favorably with many other operations generally accepted by representative surgeons. The kidney, particularly the right, is not a fixed organ, and even an excessive range of mobility is no certain index of a reflex gastric or nervous disability unless direct renal symptoms referable to the kidney are present. No diagnosis should rest solely upon palpation of an unduly movable kidney or upon a definite symptomatology unless this is confirmed by a cystoscopic examination, catheterization of the ureters, and a pyelograph to define the point of kinking in the ureter and the degree of dilatation of the renal pelvis. In their hands the Edebohl's method, with a slight modification, has proved satisfactory as a permanent means of anchorage.

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**Influence of Sun's Rays on Bone and Joint Tuberculosis.**—FREIBERG (*Am. Jour. Orthop. Surg.*, 1917, xv, 625) says from a study of 4 cases that from his experience with these 3 cases it seems inevitable to conclude that exposure to the sun's rays as here practised resulted in speedy improvement which can fairly be attributed to this agency. The retrogression which ensued upon having to abandon the systematic use of the sunlight seems to emphasize this fact and makes it desirable to continue this treatment during the winter in his own environment. The results obtained seem to indicate the value of this method even in the vicinity of large cities and at low altitudes, where, according to Rollier, who originated this treatment, the potency of the ultraviolet rays is greatly diminished by the stratum of moist and unclean air through which they must pass. It is by no means certain that the ultraviolet rays are the essentially active or the only active part of the sunlight in a therapeutic sense. In Freiberg's experience the use of the quartz ultraviolet lamp, the so-called Alpine lamp, has failed to show that it may be considered even a fair substitute for sunlight. Its light, on the other hand, is quite rich in ultraviolet rays. It seems worth while to strive to construct a form of shelter for patients which will protect them from unendurable cold, and especially humid winds, thus making possible the continuation of treatment during bright days of the whole winter season. It seems necessary to expose the whole body in order to obtain the best results. Such shelters should therefore have as covers some material permitting the easy passage of the ultraviolet rays. An investigation in this direction is under way, but has not yet yielded any result of value.

## THERAPEUTICS

UNDER THE CHARGE OF

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**Optochin in Pneumonia.**—STÜHMER (*Med. Klin.*, 1916, xii, 1286), as a result of his observations, believes that the administration of optochin is of value for the treatment of pneumonia in a certain percentage of cases. He found that in about 60 per cent. of cases it exerted a favorable influence and failed in about 40 per cent. The cases that failed to benefit by optochin therapy belonged to the more serious type of pneumonia, those which from the beginning were of doubtful outcome. He also observed that the administration of optochin is without value if a permanent fall in temperature amounting to at least  $1^{\circ}$  or  $2^{\circ}$  C. does not occur during the second day of administration. Stühmer prefers to administer the remedy by mouth in the form of the more soluble hydrochloride. He recommends as proper dosage 0.2 gram given at four-hour intervals throughout the twenty-four hours, a total of six doses daily. The patient should be watched carefully for tinnitus or impairment of hearing and the drug immediately discontinued upon the appearance of these early toxic symptoms. He observed one instance of total amaurosis following a total of 2.25 grams in a period of forty-eight hours. Patients that react favorably to optochin treatment show a fall of temperature that begins by lysis on the second day of the treatment and usually reaches normal by the fifth or sixth day. A marked beneficial effect upon the general symptoms, such as prostration, delirium and dyspnea, also followed the treatment. He enters into a theoretical explanation of the method of its beneficial action by attributing the improvement either to a simple antipyretic action or to a specific property of the drug to limit the action of the pneumococcus toxins in their ability to produce fever and general toxic symptoms. He also explains the failures of optochin therapy in certain cases by the theories that there are optochin-fast strains of pneumococci or that the drug is used in insufficient quantities and the consequent development of an optochin-fast strain results. Furthermore, the author has observed that empyema, extension of consolidation and relapses occur in patients under optochin treatment. He concludes that the drug is of some value for its antipyretic and symptomatic effects in pneumonia, but that it scarcely can be regarded as capable of improving the prognosis to life.

**A Study of Exophthalmic Goitre from the Point of View of the Basal Metabolism.**—MEANS and AUB (*Jour. Am. Med. Assn.*, 1917, lxix, 33) report the results of 224 observations on the basal metabolism in 55 cases of true toxic goitre and 20 observations in 18 cases of non-toxic goitre. They also made 37 observations on border-line cases and about



35 single observations in control cases, normal and pathological. The authors find that the toxicity as judged clinically runs very nearly parallel with the rise of metabolism. In the clinically non-toxic cases metabolism was practically normal; in the mildly toxic there was an average rise in basal metabolism of 43 per cent., in the moderately toxic of 53 per cent., and in the very toxic an average rise of 76 per cent. They concluded that the rise in basal metabolism furnishes an accurate index of the degree of toxicity in hyperthyroidism, and that it amounts to a functional test of the thyroid gland. They use their observations on basal metabolism as criteria for judging the severity and course of thyrotoxicosis and the effect of various methods of treatment. The chief therapeutic agents studied by Means and Aub were complete rest in bed, surgery, the roentgen rays, and the effect of a few drugs. It was found that rest in bed usually caused a marked fall in the basal metabolism (from +81 to +67), which continued over a period of from one to three weeks when a level or plateau was reached. This decrease in basal metabolism was not accentuated by the administration of quinin hydrobromide, veronal, paraldehyde, or triple bromides. The effect of the roentgen rays was variable: 6 patients received no treatment except the roentgen rays, and continued at their normal occupations; 2 showed no improvement; 2 were markedly benefited, and 2 showed slight improvement; 10 patients had complete rest in bed in addition to the irradiation; 6 of these showed either no improvement or else no more improvement than might be explained on the basis of rest; 2 others showed a moderate improvement. The roentgen ray proved most effective in reducing basal metabolism in the mild cases, least effective in the very severe cases. The effect of surgery was studied in 20 cases. In 12 cases observed just before and shortly after partial thyroidectomy, a striking fall in basal metabolism and toxicity occurred in every one. Some of the patients had had complete rest in bed and had reached the plateau before operation. In 6 of these the basal metabolism subsequently rose again. The effect of ligation of the thyroid arteries (2 cases) seemed to be a decrease in basal metabolism. The results of these observations suggest the following treatment of exophthalmic goitre: (a) Complete rest in bed plus irradiation should be continued until metabolism reaches a level. (b) If rest and the roentgen rays fail to restore metabolism to within 20 per cent. of the normal it is proper to resort to surgery unless there is some definite contra-indication; among contra-indications a rising metabolism, despite complete rest, seems to be very important. (c) Following operation, if metabolism again increases further active treatment should be carried out. Patients should be kept under observation for a long time—years rather than months.

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**A Method of Treatment of Mercuric Chloride Poisoning.**—WEISS (*Jour. Am. Med. Assn.*, 1917, lxviii, 1618) reports a series of 28 cases with only one fatality. The treatment is based on the Fischer theory of nephritis. In reality the treatment is a modification of that recently offered by Lambert and Patterson. Weiss gives alkali, hypertonic salts by mouth, rectum, and intravenously. By mouth he uses "Imperial Drink," made up as follows: potassium bicarbonate, 60 grains; sodium citrate, 30 grains; sugar, 60 grains; lemon or orange juice to taste to 8 ounces of water. The salts are added just before the

drink is used. Intravenously, Fischer's solution is injected. The treatment begins when the patient arrives at the hospital, which is usually within a few hours after the mercury is taken. The stomach is washed with 1 quart of milk and the whites of 3 eggs, followed by water. Before the tube is removed 3 ounces of magnesium sulphate dissolved in 6 ounces of water is introduced into the stomach. A soap-suds enema is then given. The enema and the saline cathartic open the gastro-intestinal tract and so aid in the elimination of the mercury. If the patient failed to vomit immediately after taking the poison, or if he did not receive medical attention within three hours of swallowing the mercury, an intravenous injection of Fischer's solution is given at once; 1500 c.c. may be injected if there be no cardiac involvement. The patient receives 6 to 8 glasses of "Imperial Drink" a day and "is given large quantities of water by mouth." He is allowed a liberal diet—almost anything except an excess of protein food. The analysis of the urine is used as the control of the treatment. Large quantities of urine are voided because of the large fluid intake. The urine should be kept alkaline to methyl red, for Fischer has shown that if the urine of a nephritic patient cannot be made alkaline to methyl red the patient's condition is dangerous. The almost universal albuminuria clears up more or less rapidly when sufficient alkali is introduced into the body to counteract the abnormal amount of acids produced. If the amount of urine voided is close to normal and becomes alkaline on the medication by mouth within the first twelve to twenty-four hours the intravenous injection of Fischer's solution may be omitted. If the patient's urine continues acid to methyl red, intravenous injection must be given without delay and repeated if necessary. Usually the urine becomes alkaline after three or four days. The patients are kept under treatment until the urine has been constantly alkaline from ten to twelve days and are then discharged. In only 1 patient was there any complication—a severe necrosis of the mucous membrane of the cheek and severe intestinal hemorrhage.

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**Treatment of Chronic Protozoic Enterocolitis as Encountered in the Northern United States.**—SMITHIES (*Med. and Surg.*, 1917, i, 460) points out that chronic enterocolitis associated with protozoa in the stools is more frequent in the temperate zones than is generally appreciated. In an analysis of 1000 stools examined in the Gastro-enterological Laboratory at the Augustana Hospital, viable protozoa were found in the dejecta of 93 patients. These patients came mainly from the northern half of the Central States. The source of infection was probably water, garden-truck, or fruits contaminated directly or indirectly by protozoa carriers who had at some time lived in the tropics. Chronic enterocolitis associated with protozoa must be recognized as a clinical entity even though its course in the temperate zones is not so severe and dramatic as in the tropics. Thus in the 93 cases studied by Smithies, gastric achylia was present in 43 per cent., subnormal acidity in 36 per cent., and normal or increased acidity in 21 per cent. In 70 per cent. of the cases the stools showed reduced tryptic digestion and in 29 per cent. there was deficient amylolytic ferment. Anemia suggesting the pernicious type was present in 20 per cent. and severe secondary anemia in 67 per cent. of the cases. In 74 per cent. of the cases there was an eosinophilia of 30 per cent. or more. The type of infect-

ing organism must be determined before successful treatment can be instituted and the daily microscopic examination of the stools forms the only control of therapeutic management. In Smithies's series of 93 patients 46 had multiple infection. Treatment consisted in (a) measures for freeing the alimentary tract from protozoa; (b) management of dyspepsia and malnourishment associated with enterocolitis. Measures for freeing the alimentary tract from protozoa: The patients were put on a liquid diet for two days and given each morning a glass of citrate of magnesia solution. The specific medication depends on the type of infecting organism. In entameba cases the patient is put to bed on liquid diet. To lessen the colic, hot pads moistened in boracic-alcohol solution are applied to the abdomen. For two days the patient receives per ora 10 grains of aluminum salicylate of ipecac and  $\frac{1}{3}$  grain of emetin hydrochloride hypodermically every four hours. If the stools show fewer parasites the doses of ipecac and emetin are reduced by one-third, and this is continued for another two-day period. If the parasites are still abundant no reduction is made, but usually by the end of the first week the patient receives emetin  $\frac{1}{3}$  grain twice a day and 10 grains of ipecac four times a day. The diet should be liquid or soft. In addition the colon is irrigated with 4 quarts of hot normal salt solution or a solution of quinin (1 to 3000) and thymol (1 to 5000) in normal salt solution morning and night. On the sixth day the patient is put on a fat-free diet for twenty-four hours. On the evening of the seventh day, 30 grains of thymol in honey are given at 8 P.M. and again at 10 P.M. Early next morning he receives 2 ounces of Epsom salts and throughout the morning frequent drinks of black coffee, fat-free broth, or malted milk. During the second week the emetin, ipecac, and bowel irrigations are continued, and on the evening of the tenth day two doses of thymol (15 grains each) are given. By this time the stools are usually free from parasites and the diet may be increased gradually, provided it is low in protein and not bulky. If the parasites persist at the end of two weeks the colon is irrigated with hot normal saline and from 500 to 1000 c.c. of filtered commercial kerosene are given per rectum and retained for at least an hour. If the external parts are coated with carbolated vaseline no harmful effects follow. When flagellate protozoa are the infecting organisms the treatment is much the same as for the entameba, except that no ipecac and emetin are given; instead, evening doses of calomel (5 to 15 grains) are used, followed by 2 ounces of Epsom salts next day. The calomel is repeated about every five days according to the indications furnished by the stool examinations. The management of dyspepsia and malnourishment associated with enterocolitis is treated as follows: When the stools are free from protozoa the enterocolitis is treated by large doses (30 grains) of bismuth subnitrate five times a day. Emetin and ipecac should be continued for at least six weeks and the bowel irrigations for three. The general condition of the patient is improved by the use of iron for the anemia, HCl for the subacidity, etc. The diet consists of cereals, rare meats, simple puddings, milk, and well-washed and cooked vegetables. After-treatment: Smithies believes that the protozoa may lurk in the gall-bladder and the appendix for years, and unless these are removed the patient may become a carrier or be subject to frequent reinfection. When these organs are not removed the stools should be examined at least three times a year.

## PEDIATRICS

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UNDER THE CHARGE OF

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OF PHILADELPHIA.

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**The Condition of the Reflexes in Poliomyelitis.**—REGAN (*Am. Jour. Dis. Children*, November, 1917, xiv, No. 5) states that in poliomyelitis the most common symptom is an alteration in the reflexes accompanying or following a short febrile period. The patellar reflex is the most commonly affected, owing to the frequent involvement of that region of the spinal cord which innervates the quadriceps extensor group of muscles. It was altered in 81 per cent. of 818 cases. Hyperactivity of the knee-jerks is usually, if not invariably, the first change to occur in the preparalytic stages. It may be so marked that the slightest tap with the percussion hammer will elicit a response which will cause the foot to move through the arc of a circle of from 30 to 60 degrees. The reflex, as a rule, becomes diminished and finally absent as paralysis supervenes, but it may persist exaggerated in cases in which the paralytic involvement is slight and in which the lower extremities are not concerned to any marked extent, as well as in cases that are of the spastic variety. It may also be met with when the paralysis is limited to the upper half of the body. In rare cases there may be encountered an absence of knee-jerks on the paralyzed side and an exaggeration on the opposite and healthy side. Hyperactivity of the patellar reflex is most frequent in the meningitic and ataxic cases and in the combined type of the disease in which the meningitic symptoms were prominent. Absent or normal response is the rule in purely bulbar cases except in the very early stages. An exaggerated reflex is sometimes seen in atrophied or obviously paralyzed leg. Not infrequently the knee-jerks are found hyperactive in convalescence when every other symptom of the disease has disappeared, no doubt indicative of the stage of improvement, and just preceding the return to normal. A diminished patellar reflex usually precedes its disappearance with the advent of paralysis. It may, however, persist during the entire course of the acute stage in cases with slight paralysis, especially of the meningitic and ataxic types. During the stage of improvement it is, as a rule, the first change noticed. A sluggish patellar reflex is rather unusual except in the meningeal forms of the disease. Very rarely sluggish but hyperactive reflexes are encountered. Absence of the knee-jerks is the most common alteration, and it is most frequently encountered in the myelitic and bulbar types of the malady. This symptom may be the only demonstrable objective sign of the disease. The patellar reflex may remain normal throughout the entire paralytic phase of the disease, especially in bulbar and ataxic cases. It is also common in myelitic cases when the paralysis is limited to the upper extremities and trunk. It is scarcely ever encountered when the hydrocephalus is at all marked. The plantar reflexes are exaggerated in the preparalytic stage. The hyperactivity is of a peculiar type and is accom-

panied by a response which comprises not only a movement of the foot but also of the entire leg. The reflex was altered in only 41 per cent. of 643 cases during the paralytic stage. An exaggerated response may persist into the paralytic stage, more especially in the meningitic and ataxic classes of cases. A diminished reaction was found most common in the ataxic, the myelitic, and the myelitic meningitic forms of the disease. The reflex was absent most frequently in the purely bulbar and in the bulbar myelitic types. A normal reaction was encountered most often in the ataxic, bulbar myelitic, and bulbar meningitic forms of the malady. Often the first sign of improvement in cases with the marked paralytic involvement is the gradual reappearance of the reflex. There is to be noted two types of response to the movements employed in testing for Kernig's sign, the true reaction and the other, the "pseudo-reaction" or false reaction. The true reaction is only occasionally met with, and is limited to those forms of the disease in which the meningitic symptoms are extremely prominent. The pseudo-reaction is common in all cases exhibiting a moderate or severe degree of polyneuritis, and is associated with the voluntary resistance to the extension of the leg on the thigh, owing to the pain thereby produced. It is a sign analogous to Lasigne's sign in sciatica. The Babinski phenomenon is relatively rare in poliomyelitis, but it occasionally occurs in the meningitic form of the disease. Its presence in a case in which the diagnosis was doubtful would always be decidedly in favor of tuberculosis, and, to a less extent, cerebrospinal meningitis. A true ankle-clonus is likewise very rare in contradistinction to other forms of meningitis. The reaction may be simulated in cases in which the polyneuritis is marked, owing to the severe pain caused by the movements employed. The pupillary reflex is but little altered. It may be slightly sluggish in cases with marked hydrocephalus and during the very early stage; but a reaction is almost always present except in the moribund stage. When paralysis is limited to one leg only the knee-jerks on the healthy side are more often present than absent. When the upper extremities are alone involved the patellar reflexes are more often present than absent. In a small percentage of cases of facial nerve paralysis the knee-jerks may be lost.

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. **Infantile Scurvy: A Study of its Pathogenesis.**—Hess (*Am. Jour. Dis. Children*, November, 1917, xiv, No. 5) says one of the several factors in the pathogenesis of infantile scurvy is faulty diet. In his studies pasteurized milk was found to be a contributing cause if it was not fresh; that is, if given twenty-four to forty-eight hours after pasteurization. From this point of view milk pasteurized in the city was preferable to that pasteurized at the creamery, which reaches the consumer much longer after the heating process. Aging seemed to play a greater role in the production of scurvy than heating, whether the milk was pasteurized or raised to the boiling-point. It was found that even raw milk on aging lost its antiscorbutic properties. Infantile scurvy is not a simple dietary disease. The diet is at fault in allowing the intestinal bacteria to elaborate toxins. The toxin is not always the same, and perhaps it would be better not to regard this condition as a clinical entity. Scurvy is an intestinal intoxication or auto-intoxication, due to the overgrowth of harmful bacteria in the intestines.

It is the product of an unbalanced flora which is no longer controlled by the proper dietary. Oliguria is a common symptom. The mild therapeutic effect of citric acid may be attributed to its diuretic properties. Orange-juice was found to bring about marked diuresis. One of the striking and important symptoms of scurvy is a susceptibility to infection, such as furunculosis, nasal diphtheria, "grippe," etc. Some hemorrhages are due to this secondary infection, and are to be regarded not as scorbutic but rather as focal complications. Other hemorrhages are truly scorbutic. Scurvy is essentially a disorder characterized by malnutrition and not by hemorrhages, taking months to develop, and from a clinical point of view frequently latent or sub-acute. Scurvy occurring in epidemics is described. This results when latent scurvy exists among a number of infants, and is associated with an infectious disease such as "grippe."

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**The Significance of Certain Dental Stigmata of Congenital Syphilis.**  
—WALL (*Arch. Pediat.*, October, 1917, xxxiv, No. 10) states that stigmata of inherited syphilis is evidenced by abnormalities of the permanent teeth. The virus of syphilis affecting the fetus or infant in the early months of life finds a habitat sufficiently pliable to afford a fertile field for destructive tissue change and for an equally deleterious inhibitory effect upon the tender formative structure within the alveolar processes. If the luetic poison has been in the ascendancy during certain stages of the development of the permanent teeth, especially that of dentification, the child will in later years show certain changes, such as were first brought to light by Hutchinson. This lesion of the central incisors bears his name. Other teeth as well show the stigmata of inherited syphilis, and there are other teeth which show characteristic lesions. The first permanent molar or sixth year molar presents typical deviation from the normal if the patient shows dental stigmata at all. The three dental lesions seen are Hutchinson's teeth, cuspal erosion of the first permanent molar, and dystrophies of the permanent teeth. The sixth year molar is the only permanent tooth to dentify during intra-uterine life. This occurs about the fifth to sixth month. The changes in this tooth are characteristic. There is an erosion of the grinding surface. It is irregular in form. The surface of the tooth is pitted, excavated and discolored. Often a pulpy mass of a dirty yellow color occupies most of the surface of the crown. It is sometimes called "the honey-combed molar of hereditary syphilis."

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**The Relation of the Reaction of the Urine to the Diet in Infants and Children.**—TORRES (*Am. Jour. Dis. Children*, November, 1917, xiv, No. 5). In changing the reaction of the urine in children the difficulties are diminished when a suitable diet is prescribed. By diminishing the amount of protein to 2 grams and sometimes to 3 grams per kilo the urine will often be rendered alkaline without using a drug. In cases in which the protein reaches the lowest physiological limit without rendering the urine alkaline the acidity may be diminished by adding vegetables to the diet. In older children in whom the food is more varied, much can be done by regulating the diet. The urine of carnivora is acid and that of herbivora is alkaline. The acidity in the carnivorous animals depends on the products of protein

metabolism. In cases in which vegetables are used to turn the urine alkaline, vegetables must be used in which the amount of protein is smaller in proportion to the salts, like fruits, rice, wheat and the like, rather than those in which a large amount of protein is present, such as peas, beans and the like. Vegetables which contain purins like coffee, tea and cocoa may increase the acidity, because they may produce uric acid. In cases of infection, especially of the urinary tract, and in cases of starvation, the urine tends to become more acid than in other conditions; therefore it is more difficult to render it alkaline. When drugs are used without the proper diet, the dose necessary to make the urine alkaline is much larger than is usual. The action of the drugs is very fleeting, and should be watched and given in larger and more frequent doses as necessary.

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## OBSTETRICS

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UNDER THE CHARGE OF

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**The Lower Uterine Segment.**—In a discussion before the Royal Academy of Medicine in Ireland, TWEEDY (*Jour. Obst. and Gynce. Brit. Emp.*, June-August, 1915) stated that there is now sufficient data to clear up the mystery of the anatomy of this part of the womb and the endoperitoneal tissue is the true boundary between the cervix and body, and constitutes the tendinous extremities of the uterine fibers. Until this tissue has been made inert by rupture or by opening of the internal os, no direct pressure can be brought to bear on the cervix. In fact, dilatation of the internal os is an early phenomenon in pregnancy which permits the ovum to pass through and press directly on the cervix. A continuous pressure causes a rapid hypertrophy in the cervix which does not stretch but grows.

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**Intestinal Hemorrhage in the Newborn.**—CRAWFORD (*Jour. Obst. and Gynce. Brit. Emp.*, June-August, 1915) describes 2 cases of intestinal hemorrhage in female infants, the bleeding appearing thirty-six and fifty-two hours after birth. The labors had been normal. In the first case horse serum was given subcutaneously in three doses of 2 c.c., and with each a small dose of adrenalin. This infant died on the fifth day and a duodenal ulcer was found very near the pylorus. The second case was treated by antidiphtheric serum, two doses of 5 c.c. each, followed by recovery. Breast-feeding was resumed without difficulty on the fifth day. The only symptom in both cases was free hemorrhage from the rectum and vomiting was absent. In discussion a case was described of an infant three days old that died three hours after having nose-bleeding.

**Gunshot Wounds of the Body During Pregnancy.**—SMEAD (*Am. Jour. Obst.*, December, 1916) describes the case of a patient, aged twenty-five years, pregnant, at term, who was accidentally shot in the back. The bullet entered about one inch below the twelfth rib on the right side at the outer edge of the quadratus lumborum and could be felt lying under the skin of the abdomen about two inches below the heart and to the right of the umbilicus. The patient was poorly nourished, heart and lungs normal, and urine free from albumin. There was no elevation of temperature on admission. The abdomen was hard, tense, very sensitive and slightly distended. A small quantity of blood was escaping from the wound in the back. The child's heart was strong and nearly normal in rate. Upon opening the abdomen, the peritoneal cavity contained a large quantity of free blood and coagula with which amniotic liquid was mixed. There was a perforation of the posterior wall of the uterus to the right of the midline about three inches below the fundus, and a second was present on the anterior wall about two inches below the fundus. Between the two openings the course of the bullet was about five inches. The size of the uterus made it impossible to properly explore the abdomen for intestinal perforations, and, accordingly, Cesarean section was immediately done. The placenta had been perforated by the bullet. The child was readily delivered and cried immediately. Its only injury was that the ring finger on the left hand had been broken and lacerated by the bullet. The uterus contracted normally. The uterine incision and the bullet wound were closed with chromic catgut. When the blood was sponged out of the abdomen the intestines were examined for perforations. The bullet had entered between the folds of the mesentery of the ascending colon and passed through the bowel, making two perforations. It had then gone through the uterus and into the abdominal wall without injuring the small intestine or any other organs. The perforations in the colon were closed and a drain was passed down to that on the posterior surface of the bowel. The abdomen was drained by three soft tubes; the mother made an uninterrupted recovery. The child was nursed and developed normally. The broken finger was pieced together and healed by first intention, although there was a very slight deformity. The writer has collected 29 cases, showing a surprisingly low mortality if operation is promptly performed. In discussion, Davis reported a case of a woman, pregnant three and a half months, accidentally shot by a small rifle, the bullet making twenty-one perforations in the abdominal organs. She was brought by train 85 miles to hospital and was seen twelve hours after the receipt of the injury. Five feet of intestine were removed, including nineteen perforations. The patient recovered and was delivered of a living child at the ninth month.

**Pelvic Infections in Pregnancy.**—MOORE (*Am. Jour. Obs.*, November, 1916) describes a peculiar type of pelvic infection complicating pregnancy. His patient was a rachitis negress who was delivered by Cesarean section of a living, full-term child and suffered from puerperal neuritis while in the hospital. This appeared in both arms, in the posterior tibial muscles and fingers. The patient again came into the hospital and was delivered spontaneously of a premature child which did not long survive. The patient was ill-nourished, with slightly



enlarged thyroids, and stated that there had probably been a premature rupture of the membranes and hemorrhage before she entered the hospital. Two hours after her delivery the patient had a severe chill, the temperature rising to 105° F. At three o'clock the next morning she had another chill, temperature rising to 104° F., after which it gradually declined to normal during the next twenty-four hours. The blood showed a pure growth of *Staphylococcus aureus*. The leukocytes were 11,200. On the seventh day after delivery the blood was negative but lochial discharge showed many colonies of *Staphylococcus aureus*. The patient had tenderness over the entire tibial muscles which appeared to be neuritis of a mild type. The lochia was not foul and the patient felt well during her illness.

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**Dermoid Cyst of the Ovary with Twisted Pedicle and Acute Appendicitis Complicating Pregnancy.**—DOYLE (*Am. Jour. Obst.*, November, 1916) reports the case of a primipara who had had abdominal pain at various periods of her life before marriage. Menstruation had ceased about four and a half months previously. The patient then had an attack of sharp, sudden pain in the right lower abdomen with vomiting and prostration. This lasted three days. One week later the pain again appeared on the right side and was more severe. To the right of McBurney's point and lower there was a mass of considerable size, very tender and painful. Vaginal examination was unsatisfactory. At operation an ovarian tumor was found, with two twists in its pedicle, and behind it an acutely inflamed appendix, adherent to the posterior wall of the pelvis. Both tumor and appendix were removed, the patient making an uninterrupted recovery. Pregnancy was not disturbed, and the patient ultimately gave birth to a healthy, normal child. The tumor was a dermoid filled with sebaceous material, and contained six teeth and some hair.

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**Myomectomy in Pregnancy.**—ALFIERI (*Anal. di Ostetr.*, No. 8, 1916) reviews the literature of the subject and believes that in performing myomectomy during pregnancy the operator must be sure that the substance of the uterus is not essentially damaged and that the uterus is left in such a condition as to safely perform the function of parturition. While it is desirable to practice conservatism, this must not be carried to the extent of retaining a tumor whose presence might seriously complicate labor.

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**Management of Tumors Complicating Pregnancy, Labor and the Puerperal State.**—BEACH (*Am. Jour. Obst.*, June, 1916) believes that it is of the utmost importance that the presence of ovarian tumor complicating pregnancy be early diagnosticated. The smaller the tumor the more apt it is to have torsion of the pedicle followed by gangrene. The occurrence of some acute intra-abdominal calamity during pregnancy should always suggest the possibility of a small ovarian tumor which has undergone torsion. Rupture and suppuration of such tumors may occur. As regards treatment, statistics abundantly show that operation is far safer than the expectant method. When tumors are discovered during the first half of pregnancy, unquestionably the safest

method of treatment is removal. The abdominal operation is far safer than the vaginal. When ovarian tumors are discovered during the second half of pregnancy, if the patient is at term, Cesarean section should precede or follow removal of the tumor. The writer describes the case of a girl, aged eighteen years, in her second labor, in whom it was thought there was an ovarian cyst behind the uterus complicating labor. The child was living and uterus showing high retraction ring. An attempt to replace the tumor under anesthesia failed. Upon opening the abdomen the lower segment was greatly thinned and the pedicle of a right-sided ovarian tumor passed down posteriorly behind the head into the pelvis. The tumor could be felt along the side of the head. An attempt was made to draw the tumor out of the pelvis while an assistant pushed the head up from below. This was unsuccessful and the pedicle of the tumor began to tear. With considerable difficulty a trocar was inserted into the tumor and a small quantity of mucilaginous substance was discharged. The operator then made traction on the head upward by the hand in the abdomen while an assistant made pressure on the tumor from below. This was successful. The head was then pressed down and delivered by forceps from below, followed by removal of the tumor through the abdomen. The placenta was expressed by the hand within the abdomen and the abdomen closed. Both mother and child made a good recovery. In cases of ovarian tumor complicating pregnancy and labor in which the tumor is adherent, infected or broad ligament tumor or when there is any grade of pelvic contraction, Cesarean section is the operation of choice. The tumor is dealt with after the removal of the child. In infected cases which develop late in labor, abdominal section should be at once performed. In cases in which the presence of the tumor is first discovered during the puerperal period, operation still remains the safest method of procedure.

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**Induction of Labor in Normal Pelvis at Term.**—REED (*Surg., Gynec., and Obst.*, March, 1916) argues that because the physiological duration of human pregnancy is not exactly known, and the factors that determine the onset of labor are exceedingly obscure, that one should not allow the mother to delay in pregnancy after full term has been reached. The dangers of prolonged pregnancy are overgrowth of the child, injury to mother and child, with chance of death of the fetus and considerable risk for the mother. He takes the length of the fetus as normally 50 cm. and the weight between 5 and 8 pounds. He measures the length of the child *in utero*, using a pelvimeter from the upper border of the symphysis to the breech of the child. This measurement is doubled and 2 cm. subtracted for the thickness of the abdominal wall. The result of this calculation should give the length of the child. In his cases this measurement had rarely varied more than 2 cm. from the actual length of the child obtained at birth. Müller's method of crowding the head into the pelvis may also be used to ascertain the comparative size of the pelvis and fetus. These measurements are also correct by a careful computation of the length of pregnancy taken from the menstrual history. The induction of labor is brought about after antiseptic precautions by introducing a Voorhees bag without rupture of the membranes. The bag is introduced and moderately distended, and if pains do not start

within a hour then a weight of 1 or 2 pounds is attached by a tape to the protruding tape and passed over the foot of the bed. Usually in from five minutes to half an hour contractions begin and generally go on to spontaneous expulsion. Two objections are against this procedure: One, the possibility of infection, second, the fact that a mistake in calculation may be made and the child delivered before it is thoroughly viable. Again, the dilating bag may break; 100 consecutive cases were treated in this way, 35 primiparæ and 65 multiparæ. The average duration of labor was seven hours and forty-five minutes; the shortest labor fifty-five minutes; the longest thirty hours. During, or shortly after, the insertion the bag broke six times and was reinserted three times. The average time for the expulsion of the bag was three hours and twenty minutes. The membranes were ruptured by the introduction of the bag twice. There were two maternal deaths: 1 from placenta previa with myocarditis and 1 from pneumonia eight days after labor. The average weight of the child was 7 pounds 7 ounces; the smallest 5 pounds; the heaviest 10 pounds 5 ounces. Seven children died. There were 3 cases of version and extraction; 17 cases of laceration of the perineum; forceps was used in 23 cases. In 7 patients there was postpartum rise of temperature. In but 1 case, however, was there tenderness over or beside the uterus or foul discharge or subinvolution. In only 1 case was it necessary to use the catheter after delivery. While this proposition seems attractive it cannot be endorsed by conservative obstetricians. The dilating bag often causes severe suffering, while the risk to the mother and child are greater than in spontaneous labor. This procedure disregards the natural preparation of the child for labor by its descent into the pelvic cavity. A much better criterion than the attempted measurement of the child *in utero* consists in watching the development of pregnancy, and, in primiparæ, studying the descent of the child's head into the pelvic cavity. When the patient comes to term, and this does not occur, there is some abnormality which may require the bringing on of labor. In multiparæ it is best to calculate, as accurately as possible, the period of pregnancy, and the former experience of the patient is always available for the guidance of the physician.

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**Cesarean Section for Placenta Previa.**—KRÖNIG (*Deutsch. med. Wchnschr.*, 1916, 1178, xlii), reasoning on the accepted clinical principle that not only the mother but the child must be saved, believes that version and the use of the dilating bag cannot be considered satisfactory in placenta previa. Both are exceedingly dangerous to mother and child. When the ovum is of low attachment the wall of the lower segment is infiltrated with fetal cells which sometimes cause rupture. The stretched condition of this portion of the uterus renders such operations as vaginal Cesarean section, version or dilatation, with instruments or a bag, very undesirable. When a patient with placenta previa has fever and has been tamponed on account of severe hemorrhage it may be difficult to determine just which method of Cesarean section should be chosen. Section through the body of the uterus is contra-indicated if the os is larger than a silver dollar.

## PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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**Movements of Tissues in Culture Media.**—LOEB and FLEISHER (*Jour. Med. Res.*, 1917, xxxvii, 75) give a resumé of their previous work and include some new experiments in this significant problem, which, being merely in its infancy, permits of but provisional conclusions. The authors consider three factors of importance in determining the movement of tissue cells which are brought in contact with culture media: (1) a factor recognizable for the initial sending out of pseudopodia, the primary disequilibrizing factor; (2) the contact with solid bodies which strongly influence the direction in which the cells move; (3) a centrifugal force driving the cells into the coagulum and away from the tissues. In other words, an innate centrifugal tendency and an outside factor, the stimulating action of contact with a solid body. This mode of reaction they have called *stereotropism*, which is based on surface changes occurring in cells under the influence of variations in the surrounding medium. Such modifications in the cell surface lead to a viscid condition of the ectoplasm, causing it to stick to solid bodies, thus causing the initial disequilibration as well as the movements in contact with foreign bodies, such as threads. It may be expected that the stimulus calling forth the sending out of pseudopodia affects especially that side of the cells which adjoins the coagulum (of blood plasma) while the other side adjoining the tissue is less affected. This condition itself would tend to lead to a movement in the direction of the coagulum. As to the centrifugal movement of cells away from their tissue base into the coagulum it is probable that the principal factor is the negative chematropic influence which living cells exert upon one another together with the positive attraction for the cells, exerted by certain constituents of a clot or necrotic materials, and also the mechanical factors as of contact and the polarized change in the environment of the cells. The presence of dead tissue is the factor that directly or indirectly determines the direction of movements of various kinds of cells, but this stimulus is absent under ordinary conditions in the body. Connective-tissue cells, and to a less extent differentiated epithelial cells and carcinoma, move actively in a coagulum *in vitro*, but not in the normal organism. Epithelial cells from the guinea-pig in a culture medium of coagulated blood serum were seen to grow and to divide mitotically without any association with connective tissue, behaving essentially like ameba and moving less freely than connective-tissue cells. The growth of the latter, on account of their importance in the formation of scar tissue, is of special interest. There are many factors which influence their growth into the coagulum. For this work the authors used pieces of rabbit kidney into which incisions had been made five to eleven days previous to the experiment in order to increase

the number of fibroblasts. The degree of contact between coagulum and tissue is of importance, since the fibroblasts do not grow across a space such as may be formed by the action of fibrolysins. The ingrowth of cells is more rapid if the fibers of the coagulum are parallel to those of the tissue, and the degree of hardness and the character of the surface of the coagulum are of significance; the immigration is the more difficult the denser the coagulum and the smoother its surface. The fibroblasts travel by sending out pseudopodia along the lines of the fibrils of the coagulum. The authors noticed among the fibroblasts certain ones which seemed to have a phagocytic function. As to the movement of other tissue cells in the coagulum, that of kidney tubule cells and of mouse carcinoma cells is slight. In most of these experiments growth was at its height three days after placing the tissues into the culture media; after seven days all the cells in coagulum and media were necrotic.

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**The Incidence of Bovine Infection of Tuberculosis in Man.**—Careful analyses of the infecting microorganism in tuberculosis of man are relatively few. We have gradually had it impressed upon us that the tubercle bacillus present in various tissue lesions was not always of the same kind. The attitude of Koch, in 1901, gave the impression that we need look for only one type of bacillus, the human, in studying the nature of the infective microorganism in pulmonary lesions. Newer methods of technic have given us an opportunity of studying the tubercle bacillus with greater ease, and have also opened the way for distinguishing the various types of these organisms and demonstrating their presence in human lesions. With these newer methods at hand, WANG (*Jour. Path. and Bact.*, 1917, xxi, 131) has isolated tubercle bacilli from a variety of sources. The organisms were then studied and tested to determine the type. Of 123 strains of tubercle bacilli obtained from 88 cases of tuberculosis in man, all conformed with the regular human or bovine type. Bovine bacilli were isolated 7 times in an examination of sixty-eight adults and the same microorganism was obtained 11 times from twenty children. These bovine bacilli were found in the sputum, lymph glands, abdomen, and meninges. The high percentage (55) of bovine infection in children under sixteen is striking. The author believed that the distribution of lesions as found at autopsy indicated the intestinal route of infection in 50 per cent. of the children, while in adults it fell to 13 per cent. In studying other analyses of the incidence of bovine infection in Edinburgh the author finds that in a total of 281 cases in which the type of tubercle bacillus was determined, 78 per cent. in children under five, 70 per cent. in children from five to sixteen, and 7.8 per cent. in adults over sixteen were of bovine type. The author was also able to show that tuberculous processes which had undergone calcareous change still retained some of the original infection.

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**Spirocheta Morsus Muris the Cause of Rat-bite Fever.**—Much interest has recently been shown in studies upon rat-bite fever. In all there have been over 80 cases of human infection reported in the literature. The disease in man has definite clinical manifestations, among which the periodic recurrence of the fever, swelling of lymph glands and the appearance of a skin rash are the most important. There is

usually an incubation period of from ten to twenty-two days. Schott-müller reported the finding of a streptothrix in the enlarged lymph glands of a patient, and this was subsequently confirmed by Blake, who was able to cultivate the microorganism. Shortly following this, Tunnickliff reported upon the finding of a similar streptothrix in the lungs of rats suffering from chronic bronchopneumonia. Her findings suggested that the rat was subject to spontaneous infection by this microorganism, and that during the infectious stage was capable of transferring infections to man. Shortly following the report by Blake, a brief report from Japan claimed the finding of a spirochete in the blood and tissues of 2 patients with rat-bite fever. These same authors, FUTAKI, TAKAKI, TANIGUCHI and OSUMI (*Jour. Exper. Med.*, 1917, xxv, 33) bring further evidence of the specific nature of a spirochete for this disease. They have had the opportunity of studying 5 more cases, in each of which the spirochete has been demonstrated and in 2 the microorganism was found in the circulating blood. The authors clearly point out that the disease under discussion is one having clinical manifestations as detailed above. It is pointed out that the rat may serve as a carrier for a variety of microorganisms pathogenic to man, and that the various infections may be transmitted through bites. The spirochete which they have found is larger than the *Spirocheta pallida*, and, furthermore, possesses a flagellum. With difficulty the microorganism is demonstrated directly in the lesions of man, but is more easily shown when infected tissues are inoculated into mice. Mice, rats, guinea-pigs and monkeys may all be infected. In the monkey a disease may be induced having some of the manifestations observed in the human cases. The spirochete has been successfully cultivated. Associated with this work, ISHIWARA, OHTAWARA and TAMURA (*Jour. Exper. Med.*, 1917, xxv, 45) carried on a series of animal experiments. Eighty rats were caught and were made to bite guinea-pigs. Of this number, 10 produced experimental rat-bite fever in the exposed animals. They have been unable to detect the spirochete in the mouth of the infected rats. The clinical course of the disease in the guinea-pig resembled that in man, though the progress of the fever was not as regular. The disease could be propagated to new animals by the inoculation of blood or tissue emulsions obtained from the originally infected guinea-pigs. Upon infecting rats or mice, the spirochete could be demonstrated in the peripheral blood. These authors are not as yet convinced that the spirochete which they have demonstrated is identical with that isolated by Futaki and his co-workers. The spirochetes of Ishiwarara is short and appears to possess a flagellum at each end. The spirochetes disappear from the blood of infected animals by the use of salvarsan.

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**Fistula in Ano and Tuberculosis.**—The causal relationship between fistula and tuberculosis has been a much discussed question. STONE (*Am. Rev. Tuberculosis*, 1917, i, 548) quotes Melehior as finding 61 per cent. of his fistulæ tuberculous, whereas Frey found a similar relationship in only 6.9 per cent. of 72 cases; the latter relied entirely upon a microscopic finding of a typical lesion, but the former, in addition to this, bases his figures on a diagnosis of tuberculosis elsewhere, usually in the lungs, present before, after or at the time of the fistula. Of 123

cases seen by the author, 31 were carefully examined for tuberculosis; 13 presented active lesions and 7 showed evidence of previous involvement of the lungs. Microscopic examination of tissue from 10 fistulae, all but 2 of which were from the groups which had either active or inactive tuberculosis, showed only one containing tubercles. Nevertheless, from his own experience and from that of others, he feels that there is a causal relationship between fistula and tuberculosis in 15 per cent. to 30 per cent. of the cases, while the characteristic lesion in the fistula can be demonstrated in only about 10 per cent. A corollary to this is the author's final conclusion that in a considerable percentage of cases no relationship exists between fistula in ano and tuberculosis.

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**Contributions to the Biochemistry of Pathogenic Anaërobes.**—Starting with the assumption that the effect of anaërobes is mainly local and the changes brought about lend themselves readily to analytical study, WOLF and HARRIS (*Jour. Path. and Bact.*, 1917, xxi, 386) have thrown much light on the biochemistry of *B. welchii* and *B. sporogenes*. These two anaërobes serve as examples of the saccharolytic and proteolytic groups of Henry. The authors made careful investigations on gas production, ammonia and amino-acid formation, production in tritrate acidity as well change in hydrogen-ion concentration and the sugar consumption of these bacteria with a variety of media. The methods employed are relatively simple. Different strains of the two anaërobes were used in practically all of the experiments which make it somewhat difficult to compare the various results. The results obtained are important. *B. welchii* in a medium containing 3 or 4 per cent. of lactose may give a volume of gas 3.8 times that of the medium used. Gas produced in sugar-free media such as casein is difficult to explain and the authors suggest that it may be due to the production of amino-acids which may be glycogenetic. In the experiments with peptone water prepared from casein the amino-acids appear to have provided the pabulum for gas production. The velocity of gas production shows a latent period, a sharp rise and then a secondary rise. The composition of the gas first formed was on one occasion 90 per cent. hydrogen while the relationship of hydrogen to carbon dioxide in the final composition was roughly 2.1. The activity of growth of *B. welchii* and its death are closely associated with the hydrogen-ion concentration, and it would appear that the optimum is at or below  $P_H=4.9$ , and the lethal point between  $P_H=4.52$  to  $P_H=4.56$ . The importance of the amino-acids is indicated by the increase in these substances before gas production took place. Volatile acids made up about 60 per cent. of the total acidity, and of this nearly all was normal butyric acid. The *B. sporogenes* shows many marked differences. The amount of gas produced is almost as much as that by *B. welchii*, and it produces it in practically all media. The amount of gas formed by *B. sporogenes* is the same in 4 per cent. alkaline casein and sugar in addition. The *B. sporogenes* takes longer to establish itself and produce gas on many of the media than does *B. welchii*, but during this period it is very active in amino-acid production. The proteolytic enzymes of this anaërobe attack media in which extensive proteolysis has already taken place. Ammonia was formed in one experiment

in quantities to more than balance the original amino-acids present in the medium (peptone water). In alkaline casein 20 per cent. of the total nitrogen originally present is transformed into ammonia. The strongly basic properties of ammonia are important. Butyric acid is formed by *B. sporogenes* as well as other organic acids. In conclusion, the author suggests the possibility of using a solution, for treatment of wounds with *B. welchii* present, in which the hydrogen-ion concentration is  $P_H = 4.5$ . The article is filled with suggestions for much future work and will stimulate biochemical investigations of bacterial activity.

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## HYGIENE AND PUBLIC HEALTH

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UNDER THE CHARGE OF

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**Pneumonia.**—A great advance in our knowledge of pneumonia has recently been achieved through the work of COLE (*Arch. Int. Med.*, 1914, xiv, 56), DOCHEZ and GILLESPIE (*Jour. Am. Med. Assn.*, 1913, lxi, 727), HANES (*Jour. Exper. Med.*, 1914, xix, 38), AVERY (*Jour. Exper. Med.*, 1915, xxii, 105). Four groups or strains of pneumococci are now recognized: (1) being all diplococci they can be differentiated only by their agglutination reactions with specific sera, except Group III, which is morphologically characteristic. Group I is the cause of from 30 to 47 per cent. of all cases of pneumonia and has a mortality of about 24 per cent. Group II is indistinguishable from Group I save by the agglutination reaction. It is found in from 18 to 39 per cent. of cases and is fatal in about 60 per cent. of cases caused by it. Immune sera (2) produced by each of these two groups have been obtained from horses and seem to have specific therapeutic value. Group III is the *Pneumococcus mucosus* (3) formerly classified with the *Streptococcus mucosus*. It has a distinct mucoid capsule and produces an abundant, stringy mucous growth on surface colonies. It is the cause of from 8 to 13 per cent. of all pneumonia and is fatal in about 61 per cent. of cases. Group IV comprises a heterogeneous lot of pneumococci not classified with Groups I, II or III. Each strain of cocci in this group produces a specific agglutinin for itself, which does not agglutinate the other strains or groups. This is the type ordinarily found in normal mouths. These organisms are of low virulence, cause about 20 per cent. of cases, and have a mortality of only about 7 per cent. These four groups seem quite stable and show no tendency to mutation. The pneumococci of the first three groups cause about 80 per cent. of all cases of pneu-



monia and occur only in the mouths of people recovering from the disease or of those in direct contact with such cases. In other words, pneumonia is a contact disease in at least 80 per cent. of cases, the infection being obtained from a patient or carrier.

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**Infant Mortality.**—HIBBS (*Quarterly Publications of the American Statistical Association*, December, 1915) studied the relation of infant mortality to social and industrial conditions, its recent decline in the United States, the influence of prenatal conditions and the size of the family, the relation of the mother, the effect of urban, housing, and living conditions, and the influence of economical and industrial conditions. He concluded that the fundamental cause of the excessive rate of infant mortality in industrial communities is poverty, inadequate incomes, and low standards of living, with their attendant evils, including the gainful employment of mothers. The employment of the mother in gainful occupations is simply the remedy for these evils or "adverse conditions" which the working people in industrial communities have adopted. Undoubtedly, this recourse has had an important effect on the problem, in many cases actually tending to reduce the rate of infant mortality, while in others having just the opposite effect. The primary question in considering the social causes of infant mortality is whether the employment of mothers and married women in extradomestic occupations is, from the view-point of society, as a whole, a good remedy for poverty and an acceptable means of mitigating its influence on the health and mortality of babies and young children. From the point of view of the individual or poverty stricken family the fact cannot be escaped that this effect may be both good and bad: bad, in that it causes the baby to be artificially fed, forces the mother to be absent from home, and in other ways lowers her efficiency as a mother; good, in that it increases the family income and decreases the influence of poverty. We are thus forced to conclude that the fundamental, economical and industrial factor of infant mortality is low wages. The fundamental remedy is obviously higher wages. Other remedies, such as legislation restricting or regulating the employment of mothers before and after confinement, day nurseries, the instruction of mothers and school girls in domestic economy and the like, all have their place; but the chief thing remains the provision of an adequate family income.

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**A Cheap and Efficient Liquid Disinfectant.**—A. F. STEVENSON (*U. S. Public Health Reports*, October 8, 1915) gives a method for the preparation of a new and efficient liquid disinfectant, and suggests as a name for it the "hygienic laboratory Pine Oil Disinfectant." The disinfectant is prepared from pine oil obtained by the steam or solvent process, and is emulsified with a saponified rosin in accordance with the formula given in the article referred to. Standardization experiments with a large series of tests made on different batches of the preparation showed it to have a Hygienic Laboratory phenol coefficient of from 4 to 6. The material can be prepared without the use of special apparatus. The pine oil and rosin are heated together in a covered enamelware pail until the rosin is dissolved. The mixture is cooled to 80° C., sodium hydroxide solution added, and the mixture violently

stirred for about ten minutes; sufficient water is then added to bring the mixture to the original weight. It is then quickly cooled and stored in glass or metal containers until wanted. The finished product is of a dark reddish-brown color, is rather thick and oily in appearance, free from turbidity and cloudiness, and has rather a pleasant odor, somewhat similar to turpentine. When added to water it forms a milky emulsion. Tests showed that the germicidal powers of the disinfectant remain practically constant for about two months, after which time, however, a noticeable deterioration occurs. The author claims that the disinfectant may be used wherever coal-tar compounds are used, and on account of the difficulty of obtaining upon the market the crude products for the production of coal-tar compounds, he believes that this disinfectant will come into general use.

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**The Sanitary Conditions of Hotels.**—DR. LEVERETT D. BRISTOL, Commissioner of Health of the State of Maine, announces the passage of Rules and Regulations of the State Department of Health Governing the Sanitary Conditions of Hotels. This act, approved December 31, 1917, marks Maine the first State to take legal action of a comprehensive nature in this important sanitary problem. The rules are as follows:

1. *General Cleanliness.* No garbage, manure, filth, decaying or other organic material which may serve as a breeding-place for flies or harbor the agents of infectious diseases shall be left exposed or allowed to accumulate upon any hotel or restaurant lot. For those hotels which are not in close proximity to other buildings the term lot shall be understood to include the area within 100 yards of the hotel buildings.

2. *Food.* No food shall be left exposed to dirt, flies, rats, mice, water-bugs or other vermin between such times as meals are being served or at any other time.

3. *Cold Storage.* All refrigerators or rooms in which food is kept in cold storage shall be clean and free from decaying food at all times. Such refrigerators and store-rooms shall be kept at a temperature below 50° F.

4. *Screening.* The doors and windows of all hotel and restaurant kitchens, dining-rooms and rooms where food is prepared or kept shall be adequately screened against house flies and other insects.

5. *Garbage Disposal.* All garbage and kitchen waste shall be kept in covered metal containers or otherwise adequately protected from access to flies and rats.

6. *Infectious Food Handlers.* No person having a communicable disease shall be allowed to handle or serve food. If an employee of a hotel or restaurant is suspected to be harboring the organism of any infectious disease the manager shall require such person to submit to him a certificate of health from a reputable physician or shall notify the State Department of Health by telegram of existing conditions.

7. *Washing Hands after Using Toilet.* All food handlers are required to wash their hands directly after using the toilet, water-closet or urinal, and a notice to this effect, furnished by the State Department of Health, shall be posted conspicuously in each toilet used by such persons.

8. *Clean Rooms.* All hotels shall be kept clean, in a sanitary condition, and free from noxious odors arising from any sewer, drain, privy or other source within the control of the owner, manager or agent.

9. *Clean Linen.* Every hotel shall provide each bed, bunk, cot or other sleeping place for the use of guests with clean sheets and pillow cases; and in no case after being used by one guest shall such sheets and pillow cases be used for another guest until they have been thoroughly washed and dried.

10. *Safe Water Supply.* No hotel or restaurant shall furnish to their guests water which is polluted with human or animal excrement.

11. *Analyses of Private Water Supplies.* Any private water supply in use by a hotel shall be analyzed by the State Department of Health at least once in two years and at such other times as may be required by the department, it being understood that no expense beyond express charges shall be borne by the hotel proprietor. Such water supplies shall at all times be subject to inspection.

12. *Sanitary Privies.* All privies shall be made fly-tight and kept in such sanitary condition as may be approved by the State Department of Health.

13. *Hotels.* Every hotel shall comply with the local and State laws or regulations regarding the disposal of sewage and the use of individual towels and drinking cups.

14. *Windows.* No windows in a bedroom or other public room shall be so fastened that they may not be opened to provide necessary ventilation if no other means of proper ventilation are provided. Where storm-windows are installed some provision must be made whereby access to fresh air may be easily obtained.

15. *New Management.* Whenever a hotel or restaurant changes management it shall be the duty of the new manager to notify the State Department of Health of such change.

16. *Certificates.* Upon receipt of \$3 from the management of any hotel or restaurant complying with these regulations the State Department of Health may issue a revocable certificate, expiring one year from the date on which it is issued and having the date of expiration plainly printed thereon. The certificate may be renewed upon the payment of the above-mentioned fee.

17. *Regulations Shall be Posted.* A copy of these rules and regulations shall be posted in conspicuous places where they will be frequently seen by all employees at each hotel or restaurant.

(EDITOR'S NOTE.—A rule requiring the washing of dishes in scalding hot water after each use has important hygienic value.)

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ORIGINAL ARTICLES

SURGICAL SHOCK AND SOME RELATED PROBLEMS.<sup>1</sup>

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THE subject of surgical shock has always been of deep interest to me, not alone because it is one of the unsolved problems of surgery, but because it affords to my mind such a striking example of one of the weak points in our present system of medical teaching. I mean the tendency to dislocate physiology from clinical medicine, the tendency to look upon physiology as a preparation for and not a part of. If the study of shock has taught anything, it is that the subject must be approached either by the physiologist who knows his clinical medicine or by the clinician who knows his physiology, and that physiology must be taught and learned more as a factor of the every-day practice of medicine and surgery. Anatomy is the foundation-stone of disturbed form. Pathology is in small part anatomy gone wrong; in major part it is only physiology gone wrong.

Therefore I like to talk of shock if for nothing else than to discourage the would-be surgeon. The greatest problem of modern surgery is how to make better surgeons. We may well begin by holding up before the youthful aspirants—every medical student more or less seriously contemplates the surgical career, the one and only ideal—a surgeon must know as much as any man in any branch of medicine.

<sup>1</sup> Read before the Medical and Chirurgical Faculty of Maryland, Baltimore, Maryland.

The first and chief trouble with the shock problem lies in the fact that we have no good definition. Shock is defined as a bleeding to death in the venous system of the body, that is, that in shock the blood collects in the veins, chiefly of the splanchnic system, and the patient dies because the blood fails to reach the right heart. But this disposition of the blood in shock is but a symptom, and but a symptom common to many other conditions which are not shock. It is like defining malaria as a febrile disease, characterized by regular remissions and exacerbations of temperature. Now that is what the malarial parasite does to the body, as it follows out its life cycle, but the fever is not malaria, nor is the peculiar wave-like fever malaria. The infection with this certain bug is malaria. So a definition of shock, as a bleeding to death in the veins, is only a definition of a symptom, not of a cause. A more accurate definition is, however, impossible, since we do not know the cause, therefore the next necessary step is to define and limit the definition, with the consequent result that inaccuracies, misstatements and confusions reign.

Let us agree that shock has something to do with blood-pressure and consider for a moment what blood-pressure is:

Three elements are united in the expression "blood-pressure:"

1. The pressure due to the specific gravity of the fluid itself—hydrostatic pressure.
2. The pressure caused by force exerted upon this fluid by the vessel walls and other external factors, the fluid being contained in a closed system of elastic tubes—hydraulic pressure.
3. The pressure due to movements of the fluid itself—hydrodynamic pressure.

Of these three elements the third, hydrodynamic pressure, hardly enters into a consideration of what is ordinarily included under the term blood-pressure. It is of importance in the study of certain manifestations of the transmission of pressure, such as the study of the pulse wave, but for our present purpose this hydrodynamic pressure can be left aside.

A consideration of the hydrostatic pressure of the blood leads us at once to a realization of the complexity of the factors which govern the pressure of the fluid within the blood-vascular system. It is evident that the pressure of every layer of blood must be increased by the weight of that amount of blood which lies in a vertical direction upon it, that is, considering now only the purely physical conditions and leaving all the other factors out of account. Thus the pressure of the blood in the arteries of the adult foot must be increased by the weight of a column of 165 cm. of blood (equal to 13 cm. of mercury), entirely apart from all other factors. The hydrostatic pressure in the veins of the foot and the leg is of surgical interest in the consideration of varicose veins and varicose ulcers, because varicosities are a question of hydrostatics, plus.

of course, some abnormal quality in the vein which makes them susceptible to this factor. A person with varicose veins finds relief on raising the foot to the level of the body. The varicosities appear chiefly in the veins of the subcutaneous tissue, where the veins have only the external support of this tissue. Therefore we can surgically treat and cure the condition by simply ligating these subcutaneous veins, thus forcing the blood to return by the deeper veins which lie in and beneath the muscles, and whose thin walls are strengthened by the structures which surround them on all sides.

Now normally this hydrostatic pressure is of little practical importance, since compensating devices are so well in hand, but in abnormal conditions surgery has often to think of pure hydrostatic pressure. One of the most instructive examples of the effect of hydrostatic pressure acting alone is the experiment of Hill and Barnard. If a tame rabbit be held in the vertical, head-up position, the blood will collect in the lower areas, especially the splanchnic area, and in a comparatively short time so much of the blood of the body may accumulate in this area as to cause the death of the animal from anemia of the brain. The rabbit has bled to death into the vessels of its own splanchnic area, yet we can hardly say it died of shock, for if we did our definition of shock would therefore have to be, shock is a lack of tone of the anterior belly wall; because if the experiment be tried with a wild rabbit whose abdominal muscles are strongly developed, or if the belly wall of the tame rabbit be supported by a bandage, the animal does not die.

This experiment illustrates an important point in the study of the pressure of the blood in the venous system, the enormous, almost determining factor, played by the muscles in the support of the vein walls. We must indeed look upon the body muscles functionally as a very important element of the walls of the veins themselves. It is this factor which must be considered surgically in the case of patients whose muscular system is relaxed from a long illness in bed. If they rise too quickly to a sitting position they may faint. A patient who has fainted is not to be placed in a sitting position but laid flat so that the hydrostatic pressure does not cause the blood to collect in the veins whose muscular walls, in this sense, are relaxed. A distended urinary bladder, a large cyst of the ovary, must not be emptied too rapidly or else an essential vacuum will be created into which the blood will run simply because of hydrostatic pressure.

The role played by hydrostatic pressure in the condition of shock is not clear, but it is a factor which cannot be ignored. It may indeed be that the blood collects in the veins of the splanchnic area simply because of hydrostatics; these veins are certainly the ones which have the least external support from the surrounding structures.

The hydraulic pressure of the blood is the result of a primary force produced by the contraction of the heart, acting against a resistance which is the result of the friction of a viscid fluid, chiefly in the small vessels of the periphery. What we commonly call blood-pressure is therefore the tension of the vessel wall produced by the systole of the ventricle and transmitted by an incompressible fluid. This tension of the vessel wall will depend upon the elasticity of the vessel wall and the force which stretches it. The elasticity depends upon: (1) The inherent elasticity, due to the presence of elastic membranes and fibers. Therefore the high pressure of the hardened arterics of advancing years is due to the fact that the force of the heart beat is carried straight to the periphery, not gradually taken up and absorbed by the expansion of an elastic tube. (2) The "tone" of the involuntary muscle cells, which cells persist in the smaller arteries and the arterioles, after the elastica has disappeared, and which form the most important structural element in the vessel wall of these smaller vessels. "Tone" is a term applied to that condition of the muscle cells which results in their being always stretched. If you cut any muscle the ends draw apart. This is a simple explanation of what the physiologists term "myotatic irritability," or the responsivity to the mechanical stimulus of stretching. (3) This "tone" depends upon nerve impulses and upon the presence in the circulating blood of the secretions of certain internal glands. The force acting to stretch the vessel wall will depend upon (4) The amount of blood in the vessel, which is in turn dependent upon the relation of the inflow to the outflow. The inflow will depend upon (5) the volume of blood forced out of the heart at each systole and (6) the rate of the heart beat. The outflow will depend upon the resistance, especially (7) the resistance in the arterioles and (8) the consistency of the blood. Under abnormal conditions we must also, as was just pointed out, consider the influence of (9) the hydrostatic pressure. In the background of it all there looms the omnipotent activity of (10) the vasomotor centers.

We might then define blood-pressure as a constant resulting from the summation of these ten variables, a concept which would naturally result in anything but a constant. I have mentioned these factors of blood-pressure not to impress you with the extent of my crudition, but to offer you perhaps the best explanation of why there are so many theories regarding shock. Since we do not know the cause we cannot determine upon which factor the causative agent works, and so, as in all fields of medicine where knowledge is lacking, a man will incline to the theory which fits best with his own mental process, or with the particular line of work in which he may be interested.

Thus we have Henderson, a physiologist whose chief interest is the study of the gas exchange of the body, including, of course,

the blood gases and the final interchange of gases between the tissue and blood. The importance of the exciting effect of carbon dioxide upon the vasomotor center stands out to Henderson as the one important factor, and shock is therefore a result of what he has termed acapnia, which, being interpreted, is the condition of there being not enough carbon dioxide in the blood to properly stimulate the vasomotor centers. Therefore the pressure falls. Since the carbon dioxide is a determining factor in the total acidity of the blood we next come into close personal contact with hydrogen ion concentration, and so on into the realms beyond the grasp of the simple surgical mind. The facts of carbon dioxide stimulation of the center of the vasomotor system are easily demonstrable. The opposite of this fact, a condition in which there is not enough carbon dioxide, I have never seen in my experiments, nor do I attach much weight to this theory of shock. Perhaps because I was born and raised a Presbyterian I have an abiding faith in the idea that things are arranged to meet certain ends. The breath of life is so fundamentally essential that I feel that when it fails we die, and die quickly, not by the long-drawn-out process characteristic of shock. I realize that this line of reasoning would not long stand the penetrating searchlight of serious questioning, and I trust you will take my theology simply for what it may be worth.

Now, Meltzer is a physiologist of long years' experience. He has always been deeply impressed with the forces which regulate and control activity. With every impulse to do, there comes another impulse not to do; with stimulation comes inhibition. This is perhaps best seen in the phenomena of alcoholic saturation of the body. Men do things under this pleasing stimulus not so much because of the stimulation as because of the failure of normal inhibition. There is a certain type of acute failure of the circulation doubtless referable to inhibition, seen after a blow on the chin or the larynx or the solar plexus. That normal balance between stimulation and inhibition which results in the normal heart beat is lost because of a disturbance of the inhibiting mechanism—the heart fails. This theory has this much to commend it—it certainly accounts for certain conditions which are characterized by low blood-pressure, but it as certainly does not account for all the conditions commonly called shock.

The laboratory side is not alone in inclining to an explanation of shock according to the varying ideas and ideals of the individual. The clinician has, to my mind, introduced a great element of confusion into the whole subject, not by advancing too numerous ideas as to the theory of the thing but by his tendency to herd all fatal cases in surgery into the group of shock deaths. There is perhaps a psychological reason for this. It is doubtless a greater comfort to the relatives of the deceased to feel that their beloved was taken by some mysterious act of Providence, even perhaps a



certain pride that a case of such unknown nature should have occurred in their family, than it would be to feel that the patient was called to his reward as the result of the slipping of a catgut ligature, or the slipping of the surgeon's foot just as he was pulling the kidney out of the lumbar incision.

Now, if you will recall that I mentioned ten factors which entered into blood-pressure, a disturbance of any one of which might conceivably result in death with low blood-pressure, you will understand why I feel that it would add to our understanding of the problem, especially as regards practice, if we would separate the clinical conditions, which may be followed by low blood-pressure and consequent death into four groups:

1. I would define as syncope—from *συγκοπή*, a cutting short—the condition in which the blood-pressure falls because the great automatic centers are cut off short. A blow on the head may result in immediate syncope (cutting short) if the force be sufficient to cause that condition of the cerebral centers best spoken of as *commotio cerebri*, or else a cerebral edema or a hemorrhage follows and the intracranial pressure rises until it cuts short the function of the centers. The bounding pulse characteristic of the early stages of this condition is sufficient proof that the vasomotor mechanism is performing its function. It is obvious from the practical side that in such a condition the head should not be lowered or the pressure in the cranium would be merely increased by adding the factor of gravity in the venous system to an already dangerous pressure; nor would bandaging of the limbs, nor stimulation of the vasomotors, nor infusion of salt solution be indicated. The only direct indication is to relieve this pressure on the centers.

2. I would define as collapse—*collabere*, to fall together—the condition in which by the phenomenon called cardiac inhibition the machinery of the circulation fails—the heart falls to pieces, as it were. This is the condition explained by inhibition. Here again, vasomotor stimulation is not indicated; saline infusion, bandaging of the extremities, perfusion of blood—all this is contra-indicated; the engine is stalled, and putting on more load will not start it. In fact it is not unlikely that a venesection would be more of help in this condition than any effort which would increase the burden of the heart; the poor thing, remember, is having troubles of its own.

In the third place I would put hemorrhage. Without denying that loss of blood may be a factor in the production of the condition which appeals to my mind as true surgical shock I still object to grouping deaths due to hemorrhage under the caption of deaths due to shock. Death occurs after hemorrhage because the patient bleeds to death, and I would suggest that we forget that shock has anything to do with it.

Now, having ruled out head death, heart death, hemorrhage

death, what is left to constitute the group which is true surgical shock? Obviously the problem has lost in importance. True surgical shock is to my mind the condition marked by a gradual, persistent, progressive fall of blood-pressure such as characterizes certain cases after extensive crush injury with practically no loss of blood, cases of extensive burn, and many intra-abdominal conditions, particularly high intestinal obstruction, or ileus, and acute hemorrhagic pancreatitis. These are in my opinion instances of primary failure of the peripheral vasomotor mechanism, and I further believe that they are associated in some manner with a disturbance of adrenal function. Remember that the point where the vasomotor system accomplishes its work, transforms the energy of the centers into work, is not in the venous system, nor in the capillaries, but in the arterioles, and the mechanism which transforms energy into work is the musculature of the arterioles. We know that when the adrenals have been largely destroyed by disease we have the picture of Addison's disease, a picture characterized by the asthenia of the skeletal muscles and also by the asthenia of the musculature of the arterioles, hence the consequent low blood-pressure. We know that this true form of surgical shock is especially apt to follow a manifest toxemia, as after severe burns or in hemorrhagic pancreatitis. We know that the adrenals are almost specifically affected by some toxins, as in diphtheria, and we know that the prolonged administration of chloroform or ether certainly injures the adrenals. Further, the only way in which I have succeeded in producing experimentally the condition which to me compares with surgical shock is by the complete removal of both adrenals. From the practical side we know that adrenalin, since Crile's introduction of the drug in practice, has proved valuable in the treatment of this condition.

Now, it is my belief that adrenalin produces a good effect not only because it raises the blood-pressure, for which purpose alone it was introduced, but because it supplies a something which is certainly essential to life, and in these cases is apparently lacking. The treatment of surgical shock must therefore consist in the continued administration of adrenalin plus efforts to remove the causative factor. In cases due to a manifest toxemia it is certainly only symptomatic treatment to endeavor to sustain blood-pressure and not make an effort to remove the primary toxin. This is illustrated by Hartwell and Hoguet's experiments with dogs which otherwise would have died from high intestinal obstruction in three days, but which were kept alive for ten days or longer by the use of large amounts of saline solution, probably because the toxin responsible for the death of the animal is thereby more readily eliminated. I suspect that the problem of which vasomotor stimulant to choose, whether caffeine or strychnin, etc., is probably a simple one—they are all aimed at the wrong end of the vasomotor system. Not

the vasomotor centers, but the mechanism at the periphery which transforms the energy of the vasomotor centers into work, needs stimulation; hence the good results of bandaging the extremities and using the pneumatic suit, which are mechanical supporters of the periphery, and hence the good of adrenalin, the chemical supporter of the periphery. This problem of surgical shock is primarily a clinical problem, and ought to be approached by the practical man who has not forgotten his theory.

You may have begun to wonder why I have ventured an attempt at clarifying a problem by the apparent method of making it more complex. I have done it from the stand-point of practice, for it is very clear to me that not all conditions of low pressure or shock should be treated by the same method. A patient coming with a head injury, or with an inhibited heart, or with internal hemorrhage, or with high obstruction, should not, I feel, be classed together from the stand-point of treatment. The head injury needs relief from the intracranial pressure; the heart case needs a heart stimulant and perhaps a venesection rather than transfusion; the hemorrhage case needs fluid in the vascular system, but not necessarily vasomotor stimulation; the high obstruction needs, first, removal of the toxin which is killing him, therefore washing out of the stomach and the duodenum if that is possible; washing out of the vascular system by saline solution, for the poison is in the blood; stimulation of the peripheral vasomotor apparatus, because it, too, is poisoned.

I have not as yet mentioned the doctrine of anoci-association. This is a remarkable teaching because it finds no basis in the known facts of physiology, yet it has accomplished far-reaching results in practice. The word is made up from alpha-primitive, the root of the word noxious or harmful, and association, and means the removal of all harmful impulses. The physiologist teaches that there is a constant stream of impulses from the periphery to the centers. Crile teaches that these impulses can in time wear out or fatigue the vasomotor centers and then we have shock. These external harmful impulses are especially numerous in a modern hospital. Crile holds that anoci-association begins with the doorman, and anyone who has seen the superb insolence of the average doorman will understand this point. This is undoubtedly the good of this doctrine, to treat the patient like a human being, but after the patient is under ether, those who are willing to follow Crile thus far fail to agree with him. In the first place, physiologists have been unable to produce a fatigue of the vasomotor centers after hours of peripheral sensory stimulation under ether, and secondly, it has been recently demonstrated by the use of the string galvanometer that afferent impulses do pass up the cord on sensory stimulation, but that they are abolished by ether anesthesia.<sup>2</sup>

<sup>2</sup> Forbes and Miller: *Am. Jour. Physiol.*, 1916, xl.

I would define shock as a condition marked by a gradual progressive fall of blood-pressure with no obvious cause, such as hemorrhage, intracranial pressure or heart failure. I believe that it is due to a paresis or paralysis of the musculature of the arterioles. I am aware of the fact that many think otherwise. A recent writer says: "When the development of shock is carefully investigated it is apparent that the fall of arterial pressure is caused by diminution in the output of the heart. The fall is not due to the abolition of the peripheral resistance in the arterial system. Henderson and others have pointed out that no inhibition or fatigue of any sort occurs in the vasomotor system. On the contrary, this organism is intensely active in the effort to compensate the blood stream, nor is the heart itself weakened. When the pressure in the venous system is observed it becomes evident that the apparent cardiac failure is the result of diminution of the pressure and volume of the venous stream to the right heart. The etiological sequence in certain forms of shock at least appears to be venous stasis, cardiac failure and fall of arterial pressure."

I am ready to agree that the central vasomotor nervous system shows no evidence of failure and that the heart shows no weakness, but I still believe in a primary failure of the musculature of the arterioles for several reasons:

1. They are the only parts of the vascular apparatus capable, so far as we know, of being paralyzed. The idea that the veins are dilated other than passively, implies a mechanism which has never been demonstrated.

2. A dilatation of the arterioles would necessarily be expressed in the veins because the pressure of the heart would, by this dilatation, be allowed to pass directly into the veins. There would be no congestion or stagnation in the arterioles because there must always, as long as there is any circulation at all, be a greater pressure in the arterial side than in the venous side. In this connection the fact of anatomy might be recalled, that the arterial system is empty in the cadaver.

3. The fact that physiologists find the vasomotor centers intact proves only that the centers are intact. I think they are looking at the wrong end of the vasomotor system. Why do I not go to work and prove it? Because thus far I have seen no way of demonstrating my contention. We must at any rate remember that the point where the controlling force of the vasomotor center, the energy-producing mechanism, accomplishes work, is in the arteriole. The vasomotor center is the dynamo. The nerves form the transmission system. The arteriole is the motor which transforms the energy produced by the dynamo into work.

4. What I consider shock is a manifestly toxic condition. High obstruction, acute pancreatitis, severe burns, severe infections, —crush injuries— all of these are conditions marked by the poison-

ing of the body with the toxic products of protein break-down. I suspect that these toxins injure the adrenals and the adrenals I believe are concerned in the preservation of the tone of the muscle cells of the arterioles.

5. The only way in which I have been able to experimentally produce anything which looks like shock to me is by the removal of the adrenals. After the removal of the adrenals the content of the intestinal tract contains a poison identical with, or at least similar to, the poison found in high obstruction. This fact has appeared in the work of Dr. Hendrix and myself this winter, and suggests a possible relation between high obstruction and the adrenals.

6. The relation between psychic shock and traumatic shock is compatible with my ideas. The relation between fear and anger and the adrenals is capable of experimental proof. The relation between psychic shock and that profound disturbance of metabolism known as thyrotoxicosis is universally admitted.

And, finally, my ideas of shock are entirely compatible with the best and latest in treatment. Porter,<sup>3</sup> as a result of his studies of shock at the front, advises:

1. A special position of the wounded so that the abdominal vessels shall be higher than the heart and brain (in other words, counteract the effect of hydrostatic pressure).

2. Heat. (The use of heat in shock is not clear to me. It seems like the empirical combating of a symptom, but it is universally used in practice.)

3. Intravenous injections of saline solution.

4. Intravenous injections of epinephrin. (Both of these procedures support the peripheral mechanism. Adrenalin is certainly purely a chemical supporter of the peripheral mechanism.)

5. The transfusion of blood in certain cases.

6. The observation of the diastolic pressure every half-hour, as an index of the condition of the patient. (In other words, we are dealing with a disturbance of the blood-pressure. Therefore, keep track of the blood-pressure by the only possible means, and if it be found to be failing, apply the principles of preventive medicine.)

What is the relative value of saline infusion and transfusion of blood? When should the one or the other be used? An answer to these questions must be based on personal opinion rather than on experimental or clinical fact, I think, because the men who favor any given method seem to become soon obsessed with an enthusiasm which tends to cloud the accuracy of their observations. The impartial, accurate observer is a rare bird.

The operation of transfusion of blood has a very interesting history. There are records which seem to show that the operation was practised in very ancient times. A review of an ancient Jewish

<sup>3</sup> Boston Med. and Surg. Jour., 1916, clxxv, 854.

writing which was shown to La Martinière by Ben-Israel Manasse, a rabbi of the Jews of Amsterdam, contains the following words: Naam, prince of the army of Ben-Adad, king of Syria, being attacked with leprosy, resorted to physicians who, in order to cure him, withdrew blood from his veins and replaced it with other blood. Perhaps this was not a transfusion, but early serum therapy. At a much later day, Libavius, in his treatise of the sacrifices of the Emperor Julian, speaks of transfusion as having been an eye witness of an operation of this sort.

About the middle of the seventeenth century, following upon the discovery of the circulation of the blood by Harvey in the early part of this century, together with the then prevailing philosophical conjectures concerning the real function of the blood, the question of the transfusion of blood became of unusual interest. Serious discussions were held on points such as if the blood of a sheep were transfused into a man, would he grow wool and horns, and the treatment of incompatibility of temperament (or temper) of husband and wife by mutual transfusion was seriously proposed. In the year 1667 Denis, professor of philosophy and mathematics, at Paris, performed the first transfusion operation upon a human being, that is, the first operation the account of which we find preserved in an original record. In the fall of the same year Lower and King operated in London.

The German physiologist Landois, in 1875, collected 374 cases of transfusion of human blood, of which in 150 cases the result was favorable, in 180 unfavorable, doubtful in 12, while in 3 no result was to be expected, and 2 died during the course of the operation. He also collected 129 cases of transfusion of animal blood into the human body, of which 42 resulted in a cure or continued improvement, 25 in transitory improvement or doubtful success, and 62 were followed by no improvement and death. These figures are of little value, all dating from the preaseptic days, but I give them to you to show the extent of the practice of transfusion, especially remarkable in those days in which there was relatively little surgery practised. Further, these figures show that the operation has always had a strong hold on the imagination both of the public and the surgeon, and there are more recent indications that transfusion has more often appealed to the poetic sense than to the common sense.

Landois was the first apparently to study this problem, and he arrived at two important and fundamental conclusions: (1) He observed that the mixture of the blood of two different species results in the destruction of one or both bloods—in hemolysis—and it was this work which laid the foundation for all the subsequent work on hemolysis and bacteriolysis, with the discovery of all the methods of serum diagnosis now of such invaluable aid in clinical work. Landois further demonstrated that an animal dies of

hemorrhage at a time when there are still plenty of red cells left in the body to carry on all the functions of the red cells, but when the fluid column of the blood has fallen so low that the heart cannot get a grip on this fluid column; in other words, death from hemorrhage in the normal animal results from the mechanical disturbance of the heart action rather than from the loss of a chemically vital fluid. Landois found that death after hemorrhage could be prevented if this fluid column were restored by the addition of fluid, and he introduced the method of saline infusion for the treatment of hemorrhage and shock. So saline infusion completely displaced

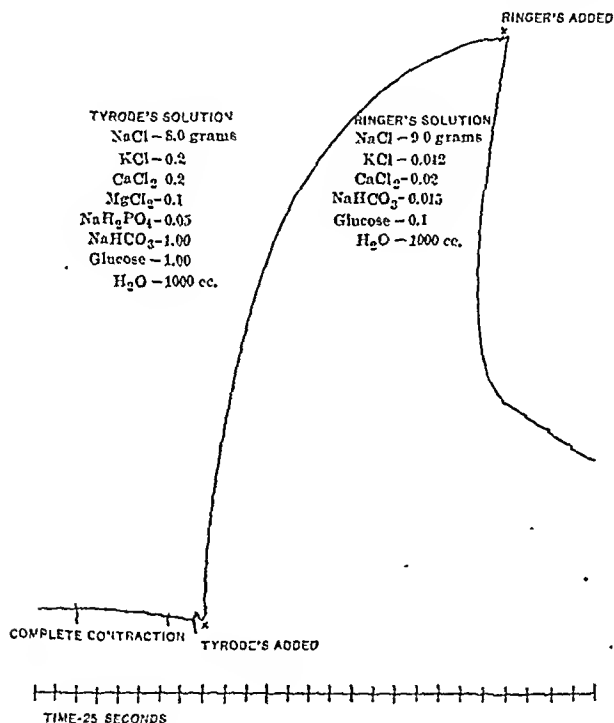


Fig. 1

blood transfusion for many years until transfusion was revived, and thus the pendulum swings backward and forward until after many swings through an arc, which gradually grows shorter and shorter, the pendulum stops at the exact center of the arc which represents the truth.

The demand for fluid by the body after hemorrhage is so insistent that fluid is taken up rapidly from the tissues, from the great serous cavities, from the stomach, intestines, the large intestine; the kidneys stop excreting. Therefore we make use of these facts in surgery. We give patients freely to drink; we inject saline into the tissues subcutaneously; we fill the large bowel with saline and

finally we inject saline directly into the veins. These methods are all of value and they differ only in the speed of attainment of the end-result.

When shall saline be used and when transfusion of blood? Now, salt solution has the great advantage of being always on hand in sterile form; a hollow needle, not too small, a rubber tube and a funnel, introducing the needle into a vein, directly through the skin—making an incision to expose the vein indicates a lack of refined technic—and the life-saving process is started. I personally firmly believe in the teaching of Landois. I feel that salt

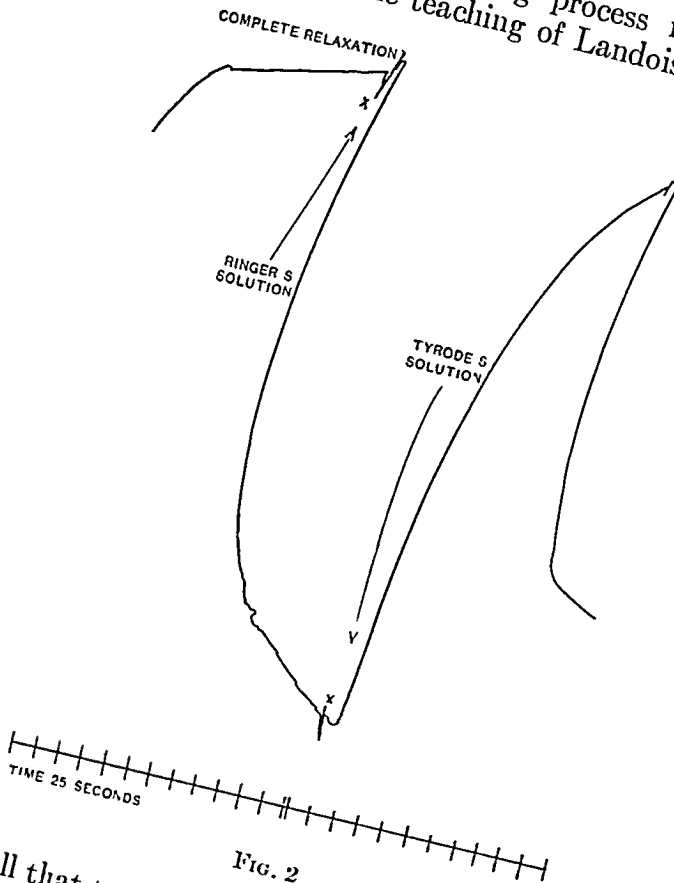


Fig. 2

solution does all that transfusion can do in the acute cases, perhaps not in the late anemias, and only two things stand out to the disadvantage of the salt solution. You may remember that I defined blood-pressure as the result of the friction of a viscid fluid in the small arteries of the periphery. Salt solution does not possess the normal blood viscosity, and it may be for this reason that it does not work sometimes. And, again, rarely, salt solution seems to leak through the lungs so rapidly as to cause acute edema. Some day I believe someone will find some colloidal addition to give saline a viscosity comparable to that of the blood, and this objection will then be done away with.



There is another point concerning salt solution which I believe worth mention. If we have learned anything from the recent work with the Dakin solution in the treatment of infected wounds, it is to my mind the fact of the importance of a surgeon's either knowing chemistry, or, since that seems to be such a disheartening task, having associated with him a real physiological chemist. Let me emphasize again the facts that I have endeavored to point out, that blood-pressure is the result of the factors found in the vessel wall, chiefly the smooth musculature, acting upon the factors found in the fluid within the vessel. A very interesting point in this relation is found in a study of the technic of using smooth muscle preparations for the testing of certain substances such as adrenalin. For this test a strip of smooth muscle is suspended in warm oxygenated Ringer's solution, and if the Ringer's solution be not exactly right all sorts of results may be expected. I have here, for example, the actual tracing made by a strip of longitudinal muscle from the small intestine of a dog which gave either complete relaxation or complete contraction, depending only on which two of Ringer's solutions was added. Therefore I venture to raise the question whether some of the untoward results obtained after saline infusion are due to the fault of the theory, or simply to the fact that the saline solution was made up by a combination of a trained nurse and a tablespoon instead of by a chemist who realized the sensitiveness of living tissue to slight changes of concentration.

Do I not then believe in transfusion of blood? I fear I am not what you would call an extreme enthusiast. Let us think for a moment of what the blood is and does and let us begin by getting out of our heads the idea that the blood is that vital life-giving fluid which can be cleaned by a spring tonic or which can become diseased with any result, from pimples on the face to cancer of the uterus. The blood is just about as vital as a bucket of water and just as full of life. It contains and carries to the tissues just what and only what the tissues put into it. It is a purely passive, inert, lifeless stream, carrying canal boats loaded with goods, the red cells, themselves again passive. The red cells are alive, yes, but only mildly so, and no more so than certain chemical agents, sponge-platinum for example. The white cells are alive in a more real sense, but they are not in the blood stream because the blood stream wants them; they were merely playing on the bank and fell in.

Please do not think I am casting aspersions on the blood. I have the highest respect for it as a common carrier, no respect at all for it as an active agent, endowed with a free will; and because I feel as I do toward the blood, I fail to see that a transfusion can ever be much more than a symptomatic treatment. You put in some fresh blood and it may do good for a little time, but I do not see how you have transferred with it any incentive to a diseased bone marrow, for instance, to brace up and lead a decent life.

One hears many favorable reports of transfusion, too many, however, like a case I recently saw. An old man, nearly seventy, suffered from a severe chronic anemia. He had several transfusions and improved somewhat. He was suffering from an extensive pyorrhea and finally had his teeth removed. He improved rather remarkably. Transfusions still were continued. Those who will may say the transfusions did it; those who will may say that the removal of the focus of chronic infection did it. All I am sure of is that the transfusions did not kill him; but after one of these transfusions he suffered a chill, and that suggests another reason why I am no enthusiast. The blood, though passive, is an extremely complex solution and suspension, and I for one have a most profound respect for any combination of physiological chemicals which require only the very slightest change to transform them from normal compounds to virulent toxins. I am frank to say that on theoretical grounds I am afraid of transfusion, and therefore consider it only an operation of last resort.

I know that there be many who will land merrily with both pedal extremities upon my ideas concerning transfusion. No doubt I am in a very small minority, a small band of wilful men. I nevertheless do not hesitate, for I feel sure that there are many who might welcome the moral support of such a minority report. I have heard within the last few weeks of two fatal cases of transfusion in the hands of good men. I would encourage the reporting of these failures of surgery, for when surgeons stop reporting successes and report only their failures, we will note an important advance. The art of surgery demands results, but the science of surgery demands the truth!

## MELANOSARCOMA OF THE RECTUM, WITH THE REPORT OF A CASE.

BY JOHN W. CHURCHMAN, M.D.,  
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THE rarity of melanotic tumor of the rectum is sufficiently attested by the fact that many surgeons of wide experience have never seen a case. The rather striking fact that the condition is not unusual in horses has long been known; but Ashton<sup>1</sup> in a treatise on diseases of the rectum and anus published in 1857 did not "know whether melanotic cancer of the rectum had been observed in man, though I have seen in the autopsy room several cases of melanotic

<sup>1</sup> On the Diseases, Injuries and Malformations of the Rectum and Anus, etc.  
London, 1857, 2d ed.

deposits in the ischiorectal fossa." The disease had, however, been recognized fairly early in man; by Virchow,<sup>2</sup> who in his Lectures on Tumors had mentioned but not accurately described a "melanotic sarcoma carcinomatodes;" by Maier,<sup>3</sup> who had described a melanotic "fasersarcom" of the anal orifice with metastases in all the organs; and by Eiselt,<sup>4</sup> who had described 2 cases. Even in 1904 Sandner<sup>5</sup> in an Erlangen thesis was able to collect only 15 cases.

The subject was, however, exhaustively studied by Chalier and Bonnet,<sup>6</sup> who publishing in 1912 and 1913 were able to assemble 64 cases; to these my own review of the literature has added 2 cases, which with my own case herewith published makes the total of reported cases to date 67.

It is certain that the anorectal region is one of the rarer sites for primary melanotic growths. Eiselt in 1860 found only 2 rectal melanoses out of 104 melanotic sarcomata and about the same figure was obtained by Dieterich in 1887. It is thus evident that the rectal melanotic sarcoma is much rarer than the ocular or cutaneous.

The history of my case is as follows: The patient was a man, aged fifty-four years. He had suffered from rectal pain for about seven months, which was not severe, however, until about three weeks before admission to the hospital. With the onset of the pain there was an increase in constipation, and physic had been required every other day for a few weeks before admission to the hospital. The appearance of some growth near the sphincter had led to a diagnosis of hemorrhoids, for which the patient had been operated in another hospital. The rectal pain, increase in constipation, and some pain along the costal margin had been the only clinical features of the disease. On examination, a flattened cauliflower-like growth could be readily felt in the lower rectum and spreading out toward the skin of the perineum. The growth was flattened out and had no definite pedicle. The finger could easily be passed above it and examination showed no mechanical reason for obstruction. In the right groin there was a large hard gland about the size of a pigeon's egg which was free from tenderness and had been present a month. No mass could be felt in the abdomen. There was no evidence on rectal examination of any involvement of the prostate or bladder in the growth. At operation the gland in the groin was first removed, and on section its gross appearance suggested a melanotic sarcoma. The abdomen was opened by an incision recently described by me. No mass was found in the descending colon or rectum, though both of these were somewhat hypertrophied. The hand was swept up

<sup>2</sup> Vorlesungen u. Geschwülste, Bd. ii.

<sup>3</sup> Berichte ü. die Verhandlungen der Gesellschaft zur Beförderung der Naturwissenschaften in Freiburg i B, 1858.

<sup>4</sup> Prager Vierteljahres Schrift f. Prakt. Heilk., 1861, Bd. lxx.

<sup>5</sup> Ein Fall von primären Melanosarkom d. Rectums, Ansbach, 1904.

<sup>6</sup> Les tumeurs melaniques primitives du rectum, Revue de Chirurgie, 1912, xlv, 914; 1913, xlvii, 64, 235, 372, 563.

over the liver which was not much enlarged but studded with nodules the size of a small marble. No other metastases could be found in the abdomen. The microscopic examination of the gland (Fig. 1), as well as of a small piece of tumor removed from the rectum (Fig. 2), showed it to be a melanotic sarcoma.

It seems fairly certain that these interesting tumors originate rather in the anorectal region than in the rectum itself, and are skin tumors primarily and mucosal secondarily. This point is pretty generally agreed upon as regards the site and origination of the new growth. As regards their histological classification there is some dispute. As Virchow's name for them ("melanotic sarcoma carcino-



FIG. 1.—Section from inguinal gland.

matodes") indicates, this dispute has concerned itself with the question as to whether these tumors should be regarded as sarcomatous or carcinomatous. It was Strohmeier, in 1844, who first called them melanotic sarcomata, Laennec's notion having been that all melanotic tumors were carcinomatous. To the former school Tuffier<sup>7</sup> among modern writers inclines. But Chancier and Bonnet, who have studied the subject exhaustively, are quite positive in their contention that melanotic tumors of the rectum are in reality anorectal epitheliomata of the Malpighian type, that they are ectodermal, having their point of origin in the anal region at the

<sup>7</sup> Arch. gén. de méd., 1858, xxx, 29.

expense of the Malpighian epithelium, that they are essentially cutaneous epitheliomata.

Many of the clinical features of these tumors are quite characteristic. They are usually situated low in the rectum, are often pedunculated, and may be either single or multiple. *The caliber of the rectum is usually little affected.* The mucosa is as a rule moveable and uninvaded, the perirectal tissue invaded. The sacrococcygeal glands are often, and the inguinal glands usually, involved: this inguinal adenopathy is often unilateral, and is the rule in melanotic, though the exception in non-melanotic, sarcomata of the rectum. In contrast with carcinoma this tumor does not tend to invade or



FIG. 2.—Section from rectal growth.

become adherent to neighboring organs. For example, the sacrum is never involved (save in cases of general metastasis) nor is the bladder or vagina. The tumor tends, however, to rapid multiple generalization. The peritoneum is usually involved, the liver in about 87 per cent. of the cases, the lungs and pleuræ in 50 per cent.; the heart, the kidneys, the skin, the retrorectal, mesenteric, retroperitoneal and other glands and, in rare instances, the intestines.

Melanotic tumors of the rectum seem to offer some exception to the rule that pigmented tumors are highly malignant. Malignant they certainly are and their malignancy is of the worst type, for it manifests itself in rapid multiple metastasis, often at great distance

from the primary growth. There are, however, cases on record in which the patient has lived and remained in good health long after the growth was discovered and operated upon. Francois-Dainville,<sup>8</sup> for instance, showed before the Anatomical Society of Paris, a patient in perfect health who had been operated on four and one-half years previously for melanotic sarcoma of the rectum. *Metastasis at a distance should be emphasized as an important feature of this disease; inguinal adenopathy associated with rectal tumors—particularly if the adenopathy is unilateral—should make one suspect a melanotic sarcoma; and in exploring from above the hand should always be first swept over the liver, to see if metastases are present. Metastases will be found in 80 per cent. of the cases, and this large group of patients will be spared an unnecessary intestinal resection.*

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## THE PROGNOSIS OF GALL-BLADDER INFECTIONS.

BY JOHN H. GIBBON, M.D.,

PHILADELPHIA.

It is well in discussing any phase of surgery of the bile passages to have in mind that practically all lesions for which surgical interference is required have their origin in infections of the mucous membrane by microorganisms. The one condition for which we most frequently operate is gall-stones, and as Sir Berkeley Moynihan so tersely expresses it, "Every gall-stone is a monument erected to the evil memory of the germ which lies buried within it." Even malignant disease of the gall-bladder, if primary, in nearly all instances has its determining cause in irritation and ulceration caused by gall-stones which themselves are the result of infection. There can therefore be no question that a microbial infection is the starting-point of nearly all the diseases of the gall-bladder for which we operate, but the type of organism, except in the acute infections or the acute stage of the infections, plays little part in the prognosis. The colon bacillus is by far the most frequent cause of the infec-

tion, and then the typhoid bacillus, the staphylococcus, and the streptococcus in the order named.

Acute cholecystitis, especially that due to the typhoid bacillus and occurring during or shortly after typhoid, is liable under proper treatment, to subside without operation, and only requires operation when there is not in a day or two a prompt subsidence of all the symptoms. The acute cholecystitis which is preceded by a history of gall-bladder symptoms extending over a considerable period of time will certainly require operation during or after the attack, and in these cases the prognosis is grave if the operation is delayed in the presence of marked and continuing symptoms of sepsis, especially if jaundice is present. The gall-bladder, when acutely infected or in an acute exacerbation of a chronic infection behaves very much as does the appendix, and the prognosis is about the same in each, excepting, of course, a perforative peritonitis is not so likely in the gall-bladder cases; but gangrene, perforation by stones of the gall-bladder and intestinal walls, acute infection of the bile ducts and the pancreas and occasionally a general peritonitis may result. I am convinced that in the majority of instances the primary infection of the gall-bladder does not give rise to the symptoms of acute cholecystitis, but that the infection occurs insidiously and the supposedly acute infection is often as a matter of fact an acute exacerbation of an old infection, due to interference with the emptying of the gall-bladder by a stone. The cases of acute cholecystitis which are not apt to subside, and which rapidly pass on to gangrene and peritonitis, are those due to the staphylococcus and the streptococcus or to complete occlusion of the cystic duct by a stone. Some of the worst cases of acute cholecystitis I have operated upon have been those in which no stone was present, but an acute infection by one of these organisms. The symptoms of severe septic infection are very marked in these cases, and if drainage of the gall-bladder is not done promptly, before the infection extends to the ducts and the liver, the prognosis is very grave. If jaundice is present it indicates a blocking of the hepatic or common duct by edema, and should add greatly to the gravity of the prognosis. If drainage is established early the prognosis is remarkably good, and if it is done late, even after gangrene has occurred, but before a general cholangitis has developed, it is not bad. It is astounding how patients recover after operations which reveal an extensive gangrenous condition of the gall-bladder and how grave the condition becomes when there is an obstruction to the flow of bile through the liver and ducts, as indicated by jaundice. I am now speaking of the acute infections without stones. When the obstruction to the flow of bile is due to the lodgment of a stone or stones which can be removed through an incision in the common duct and free drainage established the outlook is quite favorable, even in very sick patients.



As a basis for this paper I have studied my last 200 operations on the gall-bladder and ducts and have divided them into two series of 100 each. At first I thought 100 cases would be enough from which to draw conclusions, but later determined to go back over another 100 for verification and comparison of my conclusions. No case has been omitted because the lesion was not in the gall-bladder or ducts, and therefore in the list are a number of cases of cancer of the head of the pancreas and two of cancer of the stomach complicated by gall-stones. The inclusion of these cases greatly increased the operative mortality. We have also included in the mortality list a number of cases in which death did not occur for three or four months, and was due only indirectly to the operation.

So far as the cases of acute cholecystitis, in which operation was done during the height of the attack, are concerned there is no difference in the two series. In the 200 cases there were 8 cases without stone and 2 deaths, each due to septicemia, and 35 cases with stone and 10 deaths. The causes of death in these varied greatly: One was from acute hemorrhagic pancreatitis, present at the time of operation; 1 from hemorrhage from the gall-bladder and ducts two weeks after operation; 1 from suppurating pancreatitis four months after operation; 1 from pulmonary embolism three months after operation and following a thrombophlebitis of the saphenous vein; 1 from abscess of the liver and of the spleen present at the time of operation; 2 from septicemia; 1 from cirrhosis of the liver; 1 from cholangitis; 1 from acute endocarditis. These deaths comprise nearly one-half of the total number in both series of cases, and in most instances might have been prognosticated at the conclusion of the operation.

It must be apparent that an acute cholecystitis which does not promptly subside under treatment or which is characterized by severe symptoms of general infection and especially by jaundice is a very serious condition and demands prompt operation, which should comprise free drainage of the biliary tract. The cases of common duct infection, especially those in which we find the duct filled with a muddy sand which must be scooped out with a spoon, I think are the most serious cases we see excepting those complicated by an acute hemorrhagic pancreatitis. In looking over these fatal cases I have been impressed with the fact that the majority of them have been private cases and not ward cases, and that in nearly all of them there was ample warrant for operation long before the acute exacerbation of the infection occurred.

In the 200 cases cancer of the gall-bladder was found in 8 cases, and it was apparently primary in 7 of these. In but 1 case could a radical operation be done, and in this case a section of the liver was removed with the gall-bladder. The patient is alive and well today, more than four years after operation. In one of the fatal cases I was uncertain whether an obstruction of the duodenum was due to cancer or syphilis. Cancer of the pancreas was found

in 4 cases; cancer of the ampulla in 1 case and cancer of the stomach (with gall-stones) in 2 cases. In these 14 malignant cases there were 11 deaths. It is apparent then that cancer of the gall-bladder or of the pancreas carries with it a high operative mortality. Another observation of practical value is that gall-stones were responsible for nearly all the cases of primary cancer of the gall-bladder. Having accounted for 23 deaths, 12 in the acute septic cases (most of them having a cholangitis), and 11 in cases complicated by malignancy, I find 5 deaths unassigned; 1 was due to pulmonary embolism in a case of cholecystectomy; 1 to subdiaphragmatic abscess following choledochostomy; 2 to pneumonia, and 1 to complete suppression of urine.

One naturally asks whether the type of operation influences the prognosis, and I can say definitely that simple drainage of the gall-bladder in the hands of most operators is somewhat safer than cholecystectomy or the operations involving the opening of the common duct or the duodenum; but when these operations are plainly indicated simple drainage of the gall-bladder will not in most instances save the patient or relieve him of his symptoms. In my last 100 cases I have removed the gall-bladder fifty-three times and in the previous 100 cases it was removed but eleven times. In reviewing the two series I cannot discover any difference in the mortality. In the 200 cases the common duct was opened and stones removed nineteen times and the duodenum opened twice to facilitate the removal of a stone from the ampulla. In nearly all the malignant cases no operation on the gall-bladder or ducts was done.

The prognosis as to the recurrence of gall-stones is an interesting one, and my own experience leads me to believe that a true recurrence is very rare. I have operated a second time upon four of my patients for stone. In one I found a stone in the common duct which I believe was overlooked at the first operation two years previous when I had removed a great many stones from the gall-bladder and seven from the common duct. In another operated upon seven years after the first operation because of an intermittent biliary fistula I found one small stone; at the first operation the patient was very ill from a suppurating cholecystitis and cholangitis, and I had removed about 200 stones from the gall-bladder. I am rather inclined to think in this case a tiny stone was probably overlooked in the cystic duct. The third case was that of a physician who developed a recurrence of his symptoms about three years after his first operation, when I had removed 70 stones from the gall-bladder. I thought that in this case that again I might have overlooked a stone, but when I reopened the gall-bladder I found 25 soft mulberry stones, undoubtedly of recent formation. In the fourth case at the first operation I could feel no stones in the gall-bladder which appeared normal, and I did not open it. I attributed the symptoms to a band of adhesion extending from the pylorus

to the abdominal wall. Three and a half years later at the second operation I found a single gall-stone. In this case it is quite possible that the stone may have been present at the first operation. In the last 3 cases the gall-bladder was removed at the second operation. All of these cases are not included in the list of 200 under consideration, but they comprise my entire personal experience with secondary operation for stone. In but 1 case, therefore, have I seen an undoubted redevelopment of gall-stones following a primary operation for stone. This experience, I think, answers very well a query which is constantly put by the patient.

A rather interesting fact which is shown by a study of these 200 cases is that the danger of hemorrhage during and after operation on patients deeply jaundiced is practically eliminated by the prophylactic injections of horse serum. Although scores of these patients had been deeply jaundiced for varying periods of time and the coagulation time greatly reduced, there was but one death from hemorrhage, a continuous oozing from the mucous membrane. Coagulation tests are very necessary in jaundiced patients in order properly to estimate the risk of operation.

The opening and drainage of the common duct when indicated by the presence of a stone not only does not add to the risk of the operation, but if carefully carried out reduces it. The passage of inflexible probes into the ducts to ascertain if the obstruction has been entirely removed is dangerous; flushing the ducts with sterile water is a much safer method. It is much safer to open the duct than to crush the stone or forcibly push it up into the cystic duct or gall-bladder. When a stone is wedged in the ampulla it is often better to remove it through an incision in the duodenum than through the duct.

In conclusion, I would say that the mortality in gall-bladder infections depends very largely upon whether or not a cholangitis is present and that a persistent jaundice accompanied by general symptoms of sepsis is of grave import and calls for prompt drainage through the gall-bladder or common duct, or both; that a patient having undoubted symptoms of gall-bladder infection should not be allowed to postpone operation until an acute exacerbation of the infection occurs; that even far-advanced and neglected cases of infection of the gall-bladder alone give good results following operation; that jaundice due to stone in the common duct in the absence of symptoms of sepsis is not necessarily a grave symptom if prompt operation is done; that the high mortality following operations occurs in the cases of long-standing gall-bladder symptoms with acute exacerbation of the infection and in cases of malignancy of the gall-bladder and pancreas; that the use of horse serum has practically eliminated the danger of hemorrhage due to long-standing jaundice; that the recurrence of gall-stones after thorough operation is extremely rare; and finally, that more is to be learned from the study of our failures than our successes.

THE NERVOUS MANIFESTATIONS OF SYPHILIS OF THE EYE.<sup>1</sup>

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I INTERPRET your invitation to discuss the subject of the nervous manifestations of syphilis of the ocular mechanism as a request for a statement of my experience: (1) As to their frequency in neurological practice; (2) their clinical display; (3) their amenability to treatment. I have taken from the first division of the Neurological Institute the statistics of the past seven years. During that period the diagnosis of syphilis of the nervous system has been made more frequently and satisfactorily than it was in former years before study of the cerebrospinal fluid was a routine method of investigation. In approximately 4000 cases of nervous, mental and metabolic disorder there were 790 cases of syphilitic disease of the nervous system.

The accompanying tables show in a general way how these cases were distributed clinically. It should be remarked in passing that it was by design that so many were put under the general caption of cerebrospinal syphilis. It is from this group of cases that we hope eventually to differentiate recognizable clinical entities dependent upon syphilis. Syphilis of the nervous system includes diseases that have their sole origin in syphilis, such as tabes and general paresis, also many diseases that may have their origin in other causes, such as myelitis, encephalitis and arteritis. It includes also indefinite symptoms or association of symptoms variously diagnosticated, usually of the chief complaint, such as headache, insomnia, neuralgia, rheumatism, arthritis and neurasthenia. The essential lesion of cerebrospinal syphilis is lymphocytic infiltration of the pia usually associated with a circumvascular round-celled infiltration of the parenchyma immediately beneath it. This may or may not be associated with changes in the bloodvessels, and it may be of any size and distribution. Varying with its size and distribution will be the clinical display within certain limits. In certain cases this process progresses to such extent as to give rise to symptoms that justify the diagnosis meningitis: basilar, cortical, spinal. It may, on the other hand, give rise to symptoms which justify only the diagnosis of neuralgia or rheumatism or neurasthenia or any other term, popular at the time, to express malaise. It is in such cases that the designation cerebrospinal syphilis is the one that facilitates a conception of the pathological process and its treatment. For instance, it is not so very long ago that it was

<sup>1</sup> Read at a combined meeting of the New England Ophthalmological Society and Boston Society of Psychiatry and Neurology.

generally contended that the ocular palsies of tabes were of nuclear origin, while those of cerebrospinal syphilis were of root origin, but with the disappearance of the conception of so-called parasyphilitic disease this attempt at differentiation has been abandoned.

Syphilis writes its signature upon the individual whose nervous system has been invaded by the *Spirocheta pallida*, by disordering the size, shape and contour of the pupils, and in many instances by destroying their responsiveness to light and shadow. One-half of all our cases of syphilis of the nervous system were cases of tabes and general paresis, and in 335 of these 395 cases the size, shape and circularity of the pupil were disordered. Disorder of the circularity of the pupil has come to have such significance to me that in the absence of obvious attributable cause, such as iritis, scleritis or similar inflammatory conditions, it is considered suggestive of syphilis and warrant for study of the cerebrospinal fluid. It is therefore important to know whether such alterations occur in healthy individuals. It must be admitted that they do. For instance, Uhthoff found such anomalies two hundred and fifty-six times in 14,392 cases, *i. e.*, nearly 2 per cent. Others who have investigated much fewer cases found a larger percentage. Ivanoff, 9 per cent.; Mantoux, 5 per cent.; Dufour, 4 per cent.

We do not know whether the individuals upon whom these statistics were based were in reality healthy. Many cases of syphilis of the nervous system are recognized today which ten years ago were not even suspected. They are diagnosticated because we have learned empirically to suspect them, because we have given to slight pupillary abnormalities greater significance, and because we have learned the value of information given by them. Such abnormalities need not mean the existence of syphilis. They may merely indicate that syphilis had existed and had been cured.

In 467 of 790 patients it was noted that the pupils displayed the Argyll-Robertson phenomenon. It is interesting to note that in proportion to the thoroughness of examination of patients who have syphilitic disease of the nervous system is the increased frequency with which the *A-R* phenomenon has been found. Indeed, it may be said that the only infallible sign of syphilis of the nervous system is the failure of the pupil which is not fixed mechanically to react to light. In twenty-five years' experience in hospital and private practice I have never encountered an example of *A-R* pupil in non-syphilitic individuals. It should be noted here, however, that isolated cases have been recorded by Mees, Margulies, Nonne and others, in which such phenomena occurred in chronic alcoholics and in which there was no history of syphilis, and no evidences of its existence were revealed by examination of the blood serum and cerebrospinal fluid. In one case (Nonne) the examination of the tissues after death did not

reveal lesions of syphilis. Other instances of loss of the pupillary light reflex have been recorded in syringomyelia by Dejerine and Mirailhé and others, in disseminated sclerosis by Van Rad, in diabetes by Biermann, in head injury by Guillain, Franke and others, and in pineal gland tumor by Southard.

The statistics that have been often cited to support the statement that *A-R* pupils occur in non-syphilitics in which the blood serum and cerebrospinal fluid have not been examined are useless, and it only serves to obscure the issue to quote them. We now know that some cases formerly diagnosticated as syringomyelia, disseminated sclerosis and progressive muscular atrophy are sometimes founded in pathological process which has its origin in syphilis.

It may therefore be said that the *A-R* pupil bespeaks the existence of previous or existing syphilitic disease of the central nervous system. Like all rules this one may have exceptions.

What does the *A-R* pupil mean for the individual who has it? It is generally held that the prognostic significance is grave and that it heralds often a long time in advance the coming of tabes and general paresis, and other serious cerebrospinal manifestations of syphilis. In a general way this is undoubtedly true, but I have among my histories not included in these statistics no less than 22 individuals who have had *A-R* pupils for upward of five years, some as long as twenty years. In none of them has there been any indication of active syphilitic disease of the central nervous system. They are to be interpreted as indications of syphilis that has come to a stand-still spontaneously or as a result of treatment. I mention these cases particularly, as many years ago I was lessoned by one of them. A man, aged forty-five years, who had typical *A-R* pupils, and to whose family I communicated my fears of their serious significance, has remained at the head of a large organization which has required most exacting attention, and he has remained well until now, when he is beyond sixty years.

In every instance in which the *A-R* pupil is encountered accidentally, as for instance in routine ophthalmological examination, or elicited during the course of general examination, it is incumbent upon the physician to examine the blood serum and cerebrospinal fluid. In the event of their being found negative the physician is not justified in other conduct than that of watchful waiting. When evidence of syphilis is found in the blood and cerebrospinal fluid in an individual who has *A-R* pupils the condition must be looked upon as grave and calling for active and vigorous treatment, but it does not necessarily mean that the possessor of it is doomed, and it may indicate only the road he has travelled.

Dreyfus<sup>2</sup> says that isolated pupillary disturbances in syphilitics which he found in 35 to 40 per cent. of the cases should not be

<sup>2</sup> München. med. Wehnschr., 1912, No. 30.

considered of too grave pathological import. They may be merely indications of a former syphilitic infection or drenching of the nervous system which has gone on to recovery.

Assman<sup>3</sup> comes to the same conclusion that cases of isolated pupillary anomalies without alteration in the cerebrospinal fluid are not of grave significance and those with alterations in the cerebrospinal fluid are to be taken as indicative of oncoming tabes or general paresis.

It is my conviction that if 100 individuals, aged fifty years, who had syphilis during early manhood and consider themselves well, were examined that a very considerable percentage of them would be found to have pupillary anomalies which we consider to be syphilitic.

THE SYPHILITIC EYE-MUSCLE PALSIES. Next in importance to pupillary disturbances are the paralyses of the various eye muscles. Since the times when von Graefe showed that in a series of 160 cases of paralysis of the eye muscles upward of one-half of them were due to syphilis, it has been commonly stated that the origin of the ocular palsies are about equally divided between specific and non-specific causes, but since the diagnosis of syphilis has been removed from the realm of conjecture the percentage of syphilitic cases has become greater than this. In a previous paper, "Syphilis of the Brain,"<sup>4</sup> I said, "The frequency with which functions of the cranial nerves are disordered in syphilis of the brain has been habitually overstated by writers," and further experience has corroborated my belief. In the 790 cases upon which this study is based there was a history of diplopia in 150 cases, *i. e.*, in about 20 per cent. In only one-half of the number were there any evidences of third-nerve involvement when the patient was examined. In other words, the ocular palsies of syphilis of the nervous system are often transitory and disappear spontaneously or therapeutically. They are often the earliest symptoms of syphilitic disease of the nervous system, particularly of tabes and basilar meningitis, and of what we refer to in this paper as cerebrospinal syphilis. My experience does not lead me to agree entirely with Barnes.<sup>5</sup> "The ocular palsies which occur in tabes and general paralysis are in many instances permanent." Such paralyses are usually partial, transitory and amenable to treatment; in comparatively few instances permanent. In the majority of instances they are not, as formerly held, predominantly of nuclear origin.

In our statistics the third nerve showed evidence of being partially or completely paralyzed in 62 instances, and it is interesting to note that it was only affected on both sides in 5 instances. Nonne<sup>6</sup>

<sup>3</sup> Deutsch. Ztschr. f. Nervenhe., xlix, 305.

<sup>4</sup> Jour. Am. Med. Assn., July 10, 1915.

<sup>5</sup> Ocular Paralysis, Birmingham Med. Rev., lxxiii, 232.

<sup>6</sup> Syphilis of the Nervous System, second edition, p. 206.

quotes Uhthoff as expressing the opinion that bilateral involvement of the third nerve was almost as common as unilateral, but such has not been my experience. The reason for this is probably to be sought in the fact that the bulk of the material of the Neurological Institute is what might be called acute cases. Most of the cases of bilateral ocular palsy that have been published have been of long standing. Of course it should not be inferred from this that bilateral palsy of the third nerve may not occur abruptly and run an acute course. As a rule syphilitic paralysis of the third nerve is not only unilateral but partial. There are many reasons for the explanation of this, but the most important of them is by no means that which has habitually been given, namely, that the nuclei of origin of the third nerve are so extensive that their blood supply is terminal and that the fibers going to make up the trunk are so incredibly numerous that few of them may be involved without implication of the remaining constituents. The real explanation is that the lymphocytic infiltration which constitutes the essential pathological lesion of syphilis of the nervous system may vary in size, intensity and extent. To any degree and in keeping with such variation will be the implication of the motor oculi nerve or other nerves of the ocular mechanism. Total paralysis of the third nerve occurred only in 10 of our cases. This experience agrees with that of Alexander, who found 19 cases of total paralysis to 145 of partial paralysis. Total paralysis is usually either the expression of gumma which causes compression of the trunk of the motor oculi nerve at some place during its intracranial transit or of an extensive basilar meningitis.

Eye-muscle paralysis may occur alone or they may occur in combination with paralysis of other cranial nerves; sometimes no involvement of the nervous system is found save an isolated ptosis or abducens palsy. Oftentimes one finds peculiar combinations of disturbances that remain after a double-sided ocular palsy; for instance, patients who are unable to look upward, and when they try to do so convergence results, and when they try to converge they cannot. Lipschutz gives the following explanations of this: In these patients there was originally complete oculomotor paralysis, so that they could neither look up nor converge. As a part of the restorative process new fibers grew out of the central stump. These new fibers did not, however, reach the muscle for which they were originally intended, they got deflected, and instead of going to the rectus inferior they went to the rectus internus. When the patient makes the effort to look upward the impulse goes through the internus instead of the inferior. This interpretation of Lipschutz seems to have been accepted in a way by ophthalmologists. But it is not characteristic of syphilitic lesions. It may occur in any disease that destroys the roots of the nerve while the nuclei are preserved.



William G. Spiller has recorded<sup>7</sup> a case of bilateral oculomotor palsy developing after an apoplectic attack, syphilitic in origin, implicating all the muscles supplied by the third nerve in each eye. There was no implication of other cranial nerves except the optic. The occurrence of this paralysis had been preceded by a delirious state which had many features of an alcoholic delirium. He had a fall, striking the back of the head, nine years previous to the development of the eye paralysis, and two or three months after the fall he had a convulsion. At that time the pupils were Argyll-Robertson, and there was an absent left patella jerk; the oculomotor palsies were detected six weeks before he died. On autopsy it was found that the ophthalmoplegia was caused by thrombotic closure of the small arteries supplying the portion of the oculomotor nuclei near to the pons, a bilateral softening of two separate lesions confined to the nuclei of these nerves. In every case of eye-muscle paralysis, it matters not its mode of onset or its association, syphilis must be considered. It must likewise not be forgotten that even with a positive Wassermann the cause of the palsy may not be lues but tuberculosis or sinus disease. To attribute any case to rheumatism, even though the serum is negative on first examination, is hazardous. The investigation should be searching before the rheumatic origin of the disease is accepted.

Diplopia often occurs early in the course of syphilis of the nervous system and frequently is associated with only one symptom, headache. The following case is illustrative:

Woman, married, aged twenty-three years, infection three months before the occurrence of headache and dizziness. After these symptoms had persisted two months she began to have diplopia.

Physical examination showed partial paralysis of the left third and the right sixth cranial nerves. Serum Wassermann, negative; cerebrospinal fluid normal. She had three intravenous injections of salvarsan, three of neosalvarsan, ten injections of salicylate of mercury and three months' administration of iodide of potassium before she recovered.

In such a case we assume that gumma or pachymeningitis existed. It would scarcely be credible that there was nuclear involvement of the third nerve on one side and of the sixth on the other.

Paralysis of the third nerve in syphilitic disease of the nervous system is not infrequently associated with disorder of the sixth nerve; very rarely with involvement of the fourth. In this series of 790 cases the sixth nerve was involved thirty-one times; it may have been involved in other instances and have been the cause of the diplopia; in these 31 instances it was affected at the time of examination. These figures constitute a far smaller percentage than those of Ulthoff, who found in 150 cases of paralysis of the

eye muscles the sixth nerve involved twenty-seven times. Of course the reason for the infrequent involvement of the sixth nerve compared with the third nerve is its protected intracranial course and its small nuclear area. When the sixth nerve was affected simultaneously with the third nerve the lesion was usually considered meningeal.

The fourth nerve is affected in cases of syphilis of the nervous system very rarely. In five instances only was any disorder of it recorded in these statistics. In one instance it was bilateral.

The ocular disorder dependent upon syphilis may, of course, have nothing to do with the nervous mechanism of the eye. For instance, in the following case:

A woman, aged forty-five years, seen July 13, 1912, luetic infection denied. Transitory hemiplegia, abrupt onset accompanied with loss of consciousness, one-half hour's duration. Hemiplegia disappeared in twenty-four hours, and she then complained of inability to see with the right eye. Examination five days later showed traces of right hemiplegia, sluggish left pupil; inability to see with the right eye in the upper half of the field and very hazy in the lower half dependent upon hemorrhage into the vitreous.

**SYPHILITIC INFECTION OF THE OPTIC NERVES.** The optic nerve was affected more frequently than we expected. In 95 cases of the entire number the optic nerve was found to be diseased, showing inflammation, choked disk or atrophy, neuritic or simple. Among the 20 cases of cerebral meningitis papilledema was encountered five times, and in 251 cases in which the diagnosis of cerebrospinal syphilis was made it was noted seven times; in every instance the choked disk was bilateral. It is interesting to note that in 9 of the cases diagnosticated as tabes or taboparesis there was either optic neuritis or choked disk. In only 1 case of general paresis was there atrophy of the optic nerve, and in this case the tendon-jerks were exaggerated. One of the extraordinary and inexplicable things about general paresis is that it does not cause optic atrophy. Dr. W. A. Holden, ophthalmologist to the Neurological Institute, whose experiences with neurological material is perhaps greater than any ophthalmologist in this country, states that in 100 consecutive cases of general paresis with exaggerated knee-jerks examined at Ward's Island there was not one case of change in the optic nerves.

The affection of the optic nerves in syphilis of the brain, whether it be choked disk, optic neuritis or atrophy, may be the result of increased intracranial pressure, the direct effect of the meningeal proliferation or pressure from a gumma. It may likewise be due to syphilitic disease of the brain, especially of the anterior quadrigeminal or the geniculate body.

Optic neuritis or choked disk may, of course, either recover or go into atrophy.

An illustration of optic neuritis and choked disks yielding readily to treatment:

The case of a woman, aged twenty-three years, who denied knowledge of infection but who admitted a Neisser infection, began to complain of headache three months before entering the hospital in November, 1913. Soon after the headache she complained that her eyes hurt. This she thought was due to working under very strong electric light. She maintained that she had no other symptoms, but on questioning she admitted that occasionally during the past two weeks she had had diplopia. Examination was negative except for a paresis of the left superior oblique and a papilledema with hemorrhages, elevation of two diopters in each eye in the retina and four in the disks. Laboratory examination revealed serum Wassermann positive, cerebrospinal fluid Wassermann positive, globulin positive, and cells 73. She recovered promptly under salvarsan administration.

As an example of simple optic atrophy no more typical case can be cited than that of a man, aged thirty years, who denied syphilitic infection. He had been complaining for a year of failing vision and of severe headaches coming on in the early morning. Physical examination was negative save for practically complete simple atrophy of the optic nerves in both eyes. The vessels showed possibly some slight sclerotic changes. The laboratory examination was: Serum Wassermann plus, cerebrospinal fluid plus, globulin weakly plus, Fehling's plus, cells 31, and this despite the fact that he had been under constant mercurial and salvarsan treatment for nine months before he came under my observation.

In certain cases of optic atrophy accompanying syphilis it may be assumed that the lesion is of the meninges, but the diagnosis must be made without laboratory corroboration from study of the cerebrospinal fluid. For instance, in the following case:

Male, aged fifty-four years; syphilitic infection denied. Symptoms of five years' duration enumerated in the order of their development: crick in the neck; inclination to hold himself tilted to the left; pain in the outer side of the right leg from the shoe top to the knee occurring paroxysmally; loss of dexterity of the hands; universal stiffness and emaciation; failure of eyesight; haziness of memory. Physical examination negative, save the eyes. Vision 20/50 in the right eye, recognition of movements of the hand in the left. Slight diffuse pallor of both disks, and some distance from the center of right disk there were a few black patches of choroiditis. Serum Wassermann was positive; cerebrospinal fluid was negative. He made complete recovery in about six months under vigorous salvarsan treatment. Incidentally his weight increased 70 pounds.

Involvement of the trunks of the optic nerves may take place at any part of their course, but they are most liable to be affected at the chiasm, and the changes that take place in the fields as well

as in the nerve itself are most variable. As a matter of fact we are in need of careful observations of the visual fields in cases of cerebrospinal syphilis in which the optic nerve is not grossly diseased. There is practically no evidence upon which to base the diagnosis in many of these cases, save the positive Wassermann of the blood serum and the ophthalmoscopic picture. Nevertheless, I believe their origin in syphilis is secure and they should be subject to vigorous treatment. An illustrative case is briefly as follows:

A man, aged thirty-nine years, who denied syphilis, remarked toward the end of 1915 that his sight was blurred. This gradually grew worse until he had to give up his work, that of carpenter. He had no other symptoms. Examination of the eyes showed irregular pupils; the right larger than the left; the light reflex wanting; convergence reflex normal; mobility normal. Vision in the right eye 15/200, in the left 20/200. Fields showed concentric contraction of the upper half and obliteration of the lower half of the fields; more extensive in the left eye than in the right. The ophthalmoscope revealed simple atrophy of both disks. The serum Wassermann was strongly positive on five occasions. The cerebrospinal fluid was negative throughout. The diagnosis was meningitis, of syphilitic origin, causing compression of the chiasm. He received many injections of mercury and salvarsan, and although he maintains that he sees better, examination shows the vision to be the same.

In some instances, indeed, we are only justified in suspecting that the disease is of syphilitic origin, as for instance in an example of hemianopsia. A woman presented no history of syphilis save that she had had miscarriages repeatedly. In June, 1900, being then thirty-nine years old, she was seized with headache after returning from a funeral. This headache was indescribably severe, and everything seemed to her black and upside down for about nine days. After that she gradually got better, but noticed that she could not see objects to the left of her.

Examination showed no abnormalities of the nervous system; pupils slightly irregular in shape; the right larger than the left; the left responded sluggishly to light; and there was left absolute homonymous hemianopsia; vision is 20/30 to the side. The serum Wassermann and cerebrospinal fluid were negative. Examination of the heart revealed a loud, rough murmur replacing the first sound, occurring with greater intensity over the base of the heart, and a ringing second sound. The heart findings, the history of emotional distress followed by severe headaches and the way in which the symptoms came on lead us to suspect the diagnosis of cerebral embolism. However, it was recognized that the lesion to produce the hemianopsia must have been posterior to the optic chiasm and suspected that it was a syphilitic one. She was kept under close observation and two months later the serum Wassermann was

found to be positive. A month ago, seventeen years after the original attack, she had a left, incomplete hemiplegia, and the serum Wassermann was positive.

**AMENABILITY TO TREATMENT OF THE NERVOUS DISEASE OF THE EYE DUE TO SYPHILIS.** This phase of the subject must be discussed under three heads: (1) the pupils; (2) muscle paralysis; (3) diseases of optic nerve.

I have never seen an instance of disorder of the pupils caused by syphilis of the nervous system disappear spontaneously or under treatment.

Some of the muscle paralyses yield to treatment readily, others are most rebellious. The important matter is to distinguish one from the other. In a general way it may be said that the vast majority of cases of muscle paralysis associated with symptoms that justify the diagnosis of meningitis, especially those coming on abruptly, yield to treatment or recover spontaneously. On the other hand, those due to nuclear lesion (which are apt to develop insidiously) are rebellious and unamenable, but the majority of permanent ocular palsies are not of nuclear origin. Some of those that are nuclear at the end of life may have once been radicular. Some eye palsies are dependent upon destructive lesion of nerve bundles that cannot be regenerated. The longer an ocular palsy has been in existence the more unfavorable, as a rule, is the outlook. All syphilitic ocular palsies should be vigorously treated medicinally, while the blood and cerebrospinal fluid show evidence of syphilis; and after experience has shown that it is not safe to stop treatment for several months after the laboratory tests are negative.

Multiple ocular palsies indicative of diffuse lesion are quite as likely to yield to treatment as single paralysis. I have not compiled the statistics that support these statements, but such is my impression from study of the histories. Optic neuritis and choked disk unaccompanied by symptoms of increased intracranial pressure often disappear almost magically under appropriate treatment. On the other hand, we occasionally encounter cases upon which treatment has absolutely no effect and which go on to atrophy. I have never seen a case of primary atrophy yield to treatment. Nevertheless, I consider it proper to give such case treatment if there are evidences of syphilis in the blood and cerebrospinal fluid. I have seen cases of secondary atrophy improve proportionately to the disappearance of the intracranial disease, and some entirely recover.

Ophthalmologists have a unique opportunity to aid in the early detection of syphilis of the nervous system. Patients who show pupillary anomalies, particularly in size, contour and responsiveness to light, should be counselled to report to their physicians for examination of the blood serum and cerebrospinal fluid with the same seriousness as they are sent for investigation of the urine when

retinitis albuminurica is found. Finally, no case of disease of the nervous mechanism of the eye that has its origin in syphilis should be considered beyond recovery or unsuitable for treatment save primary optic atrophy that has gone on to completion.

I have never seen optic neuritis develop after the use of salvarsan such as has been described by Antonelli.<sup>8</sup>

#### WHOLE NUMBER OF CASES—790.

Tabes . . . . .	270
General paresis . . . . .	125
Cerebrospinal syphilis . . . . .	251
Syphilitic endarteritis . . . . .	28
Meningomyelitis and myelitis . . . . .	38
Cerebral meningitis . . . . .	20
Variously diagnosticated . . . . .	37
Syphilis . . . . .	21
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	790

#### TABES—270 CASES.

Disorder of size, shape and contour of pupils . . . . .	248
Loss of light reflex . . . . .	223
Changes in optic nerve . . . . .	39
History of diplopia . . . . .	53
Third-nerve involvement when examined . . . . .	21
Fourth-nerve involvement when examined . . . . .	2
Sixth-nerve involvement when examined . . . . .	13

#### GENERAL PARESIS—125 CASES.

Disorder of size, shape and contour of pupils . . . . .	87
Loss of light reflex . . . . .	42
Changes in optic nerve . . . . .	1
History of diplopia . . . . .	11
Evidence of third-nerve involvement . . . . .	6
Evidence of fourth-nerve involvement . . . . .	0
Evidence of sixth-nerve involvement . . . . .	1

#### CEREBROSPINAL SYPHILIS—251 CASES.

Disorder of size, shape and contour of pupils . . . . .	206
Loss of light reflex . . . . .	142
Changes in optic nerve . . . . .	32
Papilledema . . . . .	7
History of diplopia . . . . .	29
Evidence of third-nerve involvement . . . . .	18
Evidence of fourth-nerve involvement . . . . .	2
Evidence of sixth-nerve involvement . . . . .	9

#### CEREBRAL VASCULAR DISEASE—28 CASES.

Disorder of size, shape and contour of pupils . . . . .	22
Loss of light reflex . . . . .	16
Changes in optic nerve . . . . .	2
History of diplopia . . . . .	4
Third-nerve involvement . . . . .	2
Fourth-nerve involvement . . . . .	0
Sixth-nerve involvement . . . . .	1

<sup>8</sup> Arch. d'ophth., xxxii, 534.

## MENINGOMYELITIS AND MYELITIS—38 CASES.

Disorder of size, shape and contour of pupils . . . . .	30
Loss of light reflex . . . . .	17
Changes in optic nerve . . . . .	1
Evidence of third-nerve involvement . . . . .	4
Evidence of fourth-nerve involvement . . . . .	0
Evidence of sixth-nerve involvement . . . . .	2

## CEREBRAL MENINGITIS—20 CASES.

Disorder of size, shape and contour of pupils . . . . .	20
Loss of light reflex . . . . .	14
Papilledema . . . . .	5
Optic atrophy . . . . .	8
Third-nerve involvement . . . . .	6
Fourth-nerve involvement . . . . .	1
Sixth-nerve involvement . . . . .	4

## SYMPTOMATIC DIAGNOSIS—37 CASES.

Disorder of size, shape and contour of pupils . . . . .	24
Loss of light reflex . . . . .	13
Evidence of second nerve involvement . . . . .	1
Evidence of third-nerve involvement . . . . .	5
Evidence of fourth-nerve involvement . . . . .	0
Evidence of sixth-nerve involvement . . . . .	1

## CARDIAC SYPHILIS.

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SYPHILIS has been recognized as a cause of heart disease for several centuries, and for a long time has been thought to be an important factor in the production of arteriosclerosis and aneurysm; but until recent years heart disease was not thought to be a frequent complication of syphilis, nor has the nature of syphilitic infection of the heart been correctly understood. During the last six to eight years, however, this subject has been studied more thoroughly, and medical literature has contained a great many articles pertaining to it. In the main these articles have dealt with syphilis of the aorta rather than syphilis of the heart, but, judging by Warthin's studies,<sup>1</sup> syphilis of the heart occurs quite as frequently, if not more frequently, than syphilis of the aorta, and it would even appear that the heart is syphilitic in every individual showing good evidence of syphilis elsewhere, and possibly in some showing no gross evidence whatever of the disease.

In 1909 Wright and Richardson<sup>2</sup> demonstrated the *Spirocheta pallida* in the aortas of 5 cases of syphilitic aortitis, in every one of which the aortic valves showed more or less well-marked fibrous

changes; in 1914 Cabot,<sup>3</sup> in proposing a new classification of cases with failing heart, called one of the four types "syphilitic;" in 1915 Anders<sup>4</sup> states that rheumatism and syphilis head the list as causes of heart disease, and that some recent investigators say syphilis is the principal factor; while more recently Warthin<sup>5</sup> reports that in the pathological service of the University of Michigan, from 1912 to 1914, one-third of all the autopsy cases on adults (41) showed active syphilis on microscopic examination, of which lesions were found in the heart in 88 per cent.

Formerly these cardiac lesions were supposed to belong only to the tertiary and later stages. The lesions were thought to be mainly gummata or aneurysms or some less well-defined disease. But since the discovery of the *Spirocheta pallida* as the cause of syphilis, and of methods of staining the spirochetes in tissue, and of the Wassermann reaction as an aid to diagnosis, it has been learned that the heart may be affected in both the secondary and tertiary stages of the disease, and that the lesions are more frequently an epicarditis, endocarditis, or myocarditis.

The spirochetes appear to have a special affinity for the heart and aorta, and are found frequently in these organs in syphilis. Reuter<sup>6</sup> and Benda<sup>7</sup> and Sehmorl,<sup>8</sup> in Europe, first reported finding the spirochetes in the wall of the aorta in 1906 and 1907 and Wright and Richardson,<sup>2</sup> in this country, in 1909. Since then many others have confirmed these reports. However, Larkin and Levy<sup>9</sup> consider the demonstration of spirochetes in specimens of syphilitic aortitis as doubtful, and Longcope,<sup>10</sup> who has made a careful study of syphilitic aortitis, said several years ago that spirochetes could not be demonstrated in such lesions constantly by any means. Warthin's<sup>5</sup> painstaking and accurate studies and reports, however, prove conclusively that they can be so demonstrated, and in the tissues of both the heart and aorta. He reported last year finding the spirochetes or the characteristic tissue lesions in the hearts of a number of latent, active, and unsuspected cases of syphilis that came to autopsy, and thus pointed out the relative frequency of syphilis of the heart, as just mentioned. He found syphilis of the heart in 88 per cent. of syphilitics, while the aorta was found involved in only 78 per cent., which is contrary to the prevailing idea heretofore.

Warthin<sup>11</sup> also reported, in 1911, finding the heart wall crowded with spirochetes in congenital syphilis in nine infants and young children that came to autopsy. In eight of these syphilis was not even suspected clinically. Up to this time congenital syphilis of the heart was considered a rarity, being limited to those cases in which gumma of the heart was found; but Warthin showed that there exists a special form of diffuse interstitial myocarditis in congenital syphilis, with nothing in the gross appearance to suggest myocarditis, but with certain fibroblastic epithelioid areas of the heart wall microscopically found crowded with spirochetes. Warthin considers this



an important cause of sudden death in early life, occurring as a rule in apparently healthy children, in whom syphilis may never have been suspected clinically. In this connection Wiesner,<sup>12</sup> in 1905, reported finding syphilitic aortitis in congenital syphilitics, and Rach and Wiesner,<sup>13</sup> in 1907, found changes in the aorta in the majority of a large number of syphilitic fetuses examined; while Klotz,<sup>14</sup> in 1908, found lesions in the aorta, practically identical with those in the acquired disease, in a case of congenital syphilis that came to autopsy.

As to the nature of the syphilitic process in the heart, various authorities<sup>9 10 16 17 18</sup> practically agree that the lesion begins in all stages in the lymph spaces around the small vessels as a localized or diffuse, perivascular, small round-cell and plasma-cell infiltration, resulting in a productive inflammatory process. The evidence of these changes is plain microscopically, where there may be little or no macroscopic evidence, and the spirochetes may be found in these areas at autopsy.<sup>5 13 19</sup> Likewise, this process can be differentiated histologically from the simple degenerative process in atherosclerosis.<sup>9 15</sup>

The lesion may be situated in the epicardium, the endocardium, or the myocardium, but is more frequently found in the myocardium. In a series of 50 cases that came to autopsy, reported by Brooks<sup>16</sup> in 1913, the myocardium was diseased in 44 cases and the epicardium in 28, disease of the coronaries occurred in 35, and there was cardiac gumma in 5. Brooks does not mention the number in which endocarditis was present, but syphilitic endocarditis is known to occur frequently, and syphilis is such a well-known factor in the production of aortic endocarditis that it is to be suspected strongly in any case of aortic insufficiency. This is the most frequently encountered syphilitic valvular lesion, and occurring without involvement of any other valve, especially in patients under fifty, is extremely suggestive of syphilitic origin. Longcope,<sup>10</sup> basing his deductions upon a series of autopsy cases, found that 81.5 per cent. of cases of uncomplicated aortic insufficiency were probably syphilitic, and Larkin and Levy<sup>9</sup> state that pure aortic insufficiency is undoubtedly of syphilitic origin except in cases of infective endocarditis. When the aortic lesion is associated with a lesion of the mitral or of other valves, syphilis is less likely to be the cause, the probable origin being an infective or atheromatous process; but syphilis should be suspected until disproved. Longcope<sup>20</sup> has reported 2 cases of aortic insufficiency associated with disease of the mitral valves in which the Wassermann reaction was positive, but he states that spirochetes were not found in the mitral valves, and therefore the mitral lesion was not proved positively to be syphilitic.

Aortic insufficiency is also often associated with aortitis and sometimes with aneurysm of the arch of the aorta, both frequently the result of syphilis. Wright and Richardson<sup>2</sup> found involvement of

the aortic valve in the 5 cases in which they found spirochetes in the aorta; Larkin and Levy<sup>9</sup> state that an insufficient aortic valve is the most common complication of syphilitic aortitis, and Longcope<sup>10</sup> has frequently found the two associated, the general impression being that the valvular lesion is an extension from the aortitis. Longcope<sup>12</sup> found 4 cases of aneurysm in 43 cases of aortic insufficiency, and a similar case was seen by me within the past month at the George Washington Hospital Dispensary: A colored woman, aged twenty-eight years, with the physical signs of aortic insufficiency, and a broad supracardiac area of dulness which the fluoroscope showed to be a pulsating and expansile mass. She had a strongly positive Wassermann.

Also, lesions of other valves than the aortic are sometimes found associated with aortitis, or with aneurysm of the arch, in patients with a positive Wassermann and other evidences of syphilis, who do not give a history of rheumatism or other infection, except syphilis, that might produce endocarditis. Two such cases have been seen by me recently. In one, seen in the George Washington Hospital Dispensary, there were the signs of mitral stenosis and of aortitis in a woman, aged thirty-one years, who had a positive Wassermann and syphilitic sores in the mouth. In the other, seen in the hospital wards, there was a pulmonary stenosis associated with a beginning aortitis in a syphilitic, in whom the valvular lesion appeared to be the result of an acute endocarditis, and therefore of recent origin. If so the inference is that it was due to syphilis, though there was no absolutely definite evidence to this effect. This patient was seen by other observers, all of whom concurred in the diagnosis of pulmonary stenosis. Pulmonary stenosis is found so rarely in acquired cardiac disease that this case should be of sufficient interest to be reported briefly.

CASE REPORT.—H. H., aged twenty-eight years; white; male; married; cashier in a restaurant. This patient was sent in by Dr. Kane because of fever, headache, vertigo and nausea setting in suddenly three days before. His family history and personal history were negative. He denied syphilitic infection, but his Wassermann was four plus and Noguchi two plus. He had been married nine months and his wife had become pregnant once, resulting in a miscarriage. His temperature was irregular, ranging the first three days from 97.6° to 104.6°; the next two weeks from 98° to 101°; and then for four days from 98° to 100°, which it was when he left the hospital. Examination disclosed nothing to account for the fever other than the cardiac findings and the positive Wassermann. There was no throat or joint involvement that could be made out, nor history of any at a previous time. The cardiac impulse was in the fifth left interspace, 11 cm. from the midsternum, and the R. C. D. extended 12 cm. to the left and 3 cm. to the right of the midline. There was an area of retromanubrial dulness extending

5 cm. to the left and 2 cm. to the right in the first interspace, and 3.5 cm. to the left and 2 cm. to the right in the second interspace. There was a marked systolic thrill felt in the first, second and third spaces to the left of the sternum, most marked in the first. A soft systolic murmur was heard at the apex and transmitted faintly to the axilla; a loud, long, and coarse systolic murmur was heard over the left base, loudest in the first left space, also a faint systolic murmur was heard in the aortic space and in the neck. These murmurs and the thrill were scarcely recognizable at the first examination, later increased in intensity, and varied much in intensity from time to time. The aortic second was distinct, the pulmonic second faint. The blood-pressure was 124 systolic and 64 diastolic in the left arm and 126 systolic and 58 diastolic in the right arm (Tycos). The pulse was regular in force and frequency, 64 to 100, generally between 80 and 90. There was no tracheal tug and pulsation in the radials was synchronous. The blood, on admission, showed 80 per cent. hemoglobin, 4,200,000 red cells, and 8900 leukocytes; 65 per cent. polymorphonuclear neutrophiles and 4 per cent. eosinophiles, 10 per cent. small and 20 per cent. large lymphocytes, and 1 per cent. transitionals. One week later there were 11,200 leukocytes. The Widal was negative and the malarial parasite was not seen in four examinations. A roentgen ray by Dr. J. H. Selby showed an area of increased density in the first and second spaces, comparing accurately with the area of dulness in this region, and the fluoroscope showed no expansile tumor. He was given one deep injection of salicylate of mercury, which produced salivation promptly, and two doses of salvarsan, but did not seem to be particularly benefited. He left the hospital at his own request, and, unfortunately, has been lost sight of.

The time at which the heart lesion becomes manifest varies and cannot always be determined, but Brooks<sup>16</sup> states that serious involvement of the heart may begin before or with the secondary stage, and that lesions in the heart frequently appear early. In one case in Brook's series death resulted from a minute perforation of the aorta just above the ring before the secondary rash had fully appeared and before the diagnosis had been made. Other instances of early cardiac syphilis have been recorded, but not many. In this connection I wish to mention a case recently seen by me:

A young man, aged twenty-four years, referred by Dr. Garnett for examination because of precordial pain of a few days' duration, had a temperature of 99.6° and a pulse rate of 110, a slightly enlarged area of cardiac dulness, an occasional extrasystole and a soft systolic murmur at the base. There was a beginning macular eruption over his body, which he had not noticed until it was pointed out to him at that time. He denied knowledge of luetic infection, but acknowledged possible exposure to infection. His Wassermann was strongly positive. Since getting antiluetic treatment his

cardiac symptoms have subsided. Therefore this would appear to be a case of syphilis with cardiac involvement occurring early in the secondary stage.

The cardiac involvement is not often recognized at this early stage, however. The majority of cases of cardiac syphilis are discovered at a later period, owing, probably, to the fact that the symptoms of cardiac syphilis in the early stages are not very definite, and to the fact that the relation between such cardiac symptoms and syphilis is not generally understood. Possibly, too, though infection of the heart occurs early, the process may remain latent for years.

Precordial pain, palpitation, dyspnea, tachycardia, with intermittence, extrasystole or other disturbance of rhythm, more marked on slight exertion, together with a soft systolic murmur at the apex, are very suggestive of cardiac involvement even when history of the infection is denied. Grassman,<sup>21</sup> in his study of the vascular system of 288 cases of secondary syphilis, states that in 85 per cent. there were disturbances in the rate and rhythm of the pulse, while accidental murmurs, usually with dilatation of the heart, occurred in 40 per cent. With the secondary stage, in addition to the symptoms directly referable to the heart, there also are symptoms of a mildly acute infectious disease, slight fever with a moderate leukocytosis often and a relative polymorphonuclear increase. Later in the disease, after a longer cardiac involvement, the earlier cardiac symptoms having been overlooked possibly, the symptoms are those of an acute or more usually a chronic endocarditis, generally of the aortic valve; or of myocarditis; or of angina, due possibly to partial occlusion of the coronary arteries; or of heart-block.

The diagnosis will depend upon these signs and symptoms of some cardiac disorder, together with the history, the general aspects of the case, the Wassermann, and the response to specific medication. Possibly the most important single element is a positive Wassermann. In a study of 36 cases of aortic disease, in 1912, Cummer and Dexter<sup>22</sup> found a positive Wassermann in 27, or 75 per cent.; and out of 47 cases examined by Longcope<sup>10</sup> 35, or 74.4 per cent., gave a positive reaction. Seven of these positive cases came to autopsy, and all showed typical mesaortitis with involvement of the aortic ring, while in 3 spirochetes were found in the wall of the aorta. Larkin and Levy<sup>9</sup> state that 94 per cent. of individuals with luetic aortitis give a positive Wassermann. Similar reports are to be found, the percentage of positive Wassermans being variously given. Longcope,<sup>10</sup> in summing the matter up, gives from 25 to 68 per cent. positive in general cardiovascular disease, from 75 to 80 per cent. positive in aortic insufficiency, from 85 to 95 per cent. positive in aneurysm, and from 75 to 88 per cent. positive in aortic disease in general. As stated before, the signs of aortic insufficiency, unassociated with other valvular lesions, in an individual under fifty are practically pathognomonic of cardiac syphilis, when

infective endocarditis can be excluded; and the association of any valvular lesion with an aortitis or an aneurysm of the arch of the aorta in a person with a positive Wassermann, in whom rheumatism can be excluded, is, to my mind, to be looked upon with great suspicion. Anginal attacks suggest disease of the coronaries or cardiac aneurysm, and the possibility of syphilitic etiology in this event, especially in persons under fifty, should be carefully investigated. The so-called cardiac crises in tabes are probably anginal attacks from coronary disease, so frequently the result of syphilitic infection of these vessels. Warthin<sup>5</sup> believes that the heart and aorta of every latent syphilitic are involved, and that syphilis will be found to be the principal factor in the production of myocardial insufficiency and the cardiovascular renal complex. From his studies it is to be inferred that when syphilitic aortitis exists there exists also syphilitic involvement of the heart, and, also, contrary to the general impression, that the cardiac lesion is not necessarily incidental to the aortitis. This aortitis may be recognized by increased retromanubrial dulness, a broad roentgenographic shadow in this region, possibly increased systolic blood-pressure, a systolic murmur at the base transmitted to the neck as a rule, and a positive Wassermann.

A cure of cardiac syphilis is hardly to be expected under any circumstances, but an amelioration of the symptoms and a prolongation of life in comparative comfort may be expected when proper treatment is instituted early. Even in late cases proper treatment will do much good, but after cardiac decompensation has set in it is unusual for any treatment to do more than slight good, and such cases usually end fatally within a comparatively short time. There were 2 cases with decompensation in the George Washington University Hospital wards recently. One derived no benefit from any treatment and ended fatally in a short time; the other improved somewhat under rest, digitalis, mercury, and salvarsan, and left the hospital, but was never able to return to work, and has again more recently returned to the hospital for further treatment. Brooks and Carroll<sup>17</sup> state that when treatment has been interrupted, as in this instance, and is later resumed again, one rarely gets as prompt and satisfactory a response. This observation is exemplified in this patient.

Treatment of cardiac syphilis should be mainly antisiphilitic and intensive. It should differ but little, if at all, from the treatment of syphilis generally, except in so far as the cardiac involvement may be seen to be affecting the patient. The principal object should be to destroy the spirochetes in the tissues as quickly and as effectively as possible, and therefore antisiphilitic treatment should be pushed to the limit of tolerance. As to specific medication, there can be no cut-and-dried rules that will apply to all cases. Each case must be treated individually. Mercury by deep injection, preferably

one of the soluble salts, and salvarsan intravenously are both to be used. There appears to be but little choice between the old and the new salvarsan, but personally, from a rather limited observation, I am inclined to prefer the old. There is some question as to the use of salvarsan in acute endocarditis, but used in small dose often repeated, rather than in full dose, I believe it to be safe. The iodides are apparently of no use in the early cases, though possibly helpful in old lesions. Improvement is prompt, as a rule, in all cases, though, of course, more marked in early cases, and cardiac decompensation always offers a poor prognosis. In the early cases the patients must avoid cardiac strain until their cardiac symptoms are in abeyance; otherwise cardiac treatment is not indicated. In long-standing cases, when circulatory disturbance is more marked, improvement often takes place promptly under specific treatment alone, but, as a rule, it is almost always advisable also to place these patients under the usual hygienic and therapeutic treatment indicated by the circulatory condition, mainly rest and digitalis.

According to Brooks and Carroll, Anders and others treatment should be continued for at least one year after all signs of activity have subsided, and, irrespective of a negative or a positive Wassermann, antispecifics should be administered from time to time throughout life.

**CONCLUSIONS.** Cardiac complications during syphilis occur much more frequently than has been recognized generally heretofore.

The cardiac lesions occur earlier in the disease than has been thought, even in the early secondary stage.

Congenital syphilis of the heart is a cause of sudden death in early life, this condition being unsuspected clinically, as a rule.

The nature of the process in the heart is distinct and may be recognized microscopically, and the spirochetes may be found in the lesion; it is most frequently a myocarditis. Uncomplicated aortic insufficiency is of syphilitic origin in the majority of instances.

The symptoms are not definite but extremely suggestive; the diagnosis depends mainly upon the signs of some cardiac disorder, with a positive Wassermann, and a response to antiluetic treatment.

The prognosis is good in the early stages and varies directly with the stage of the disease and the extent of the changes produced.

Treatment should be mainly antisymphilitic and intensive. Cardiac treatment is required rarely except in cases with decompensation. Once instituted treatment should be carried through persistently and uninterruptedly.

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## SULPHOCONJUGATION AS A TEST OF LIVER FUNCTION.

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OF the various functions of the liver, its detoxicating influence is one of the most important, and one also, to which very much attention has been devoted. It is quite well known that toxic radicals liberated during the process of normal or abnormal intestinal digestion are carried to the liver by means of the portal circulation, and there either neutralized or oxidized or conjugated, etc., to lessen or remove the toxic influence of the substance. One of these methods of detoxication is the union of aromatic radicals with sulphuric acid and their excretion in the form of conjugated sulphates (ethercal sulphates) in the urine.

Since Städeler found phenol in cows' and horses' urine, Landolt, Lieben, Hoppe-Seyler, Buliginsky, and Munk found traces of it in normal human urine, and Salkowski observed that in ileus and other obstructive intestinal disease the excretion of phenol in the urine is much increased.

This formation of phenol and phenolic substances, cresol, indol, skatol, etc., has been ascribed to the action of intestinal bacterial flora. Such organism like the *B. coli communis*, which is a normal inhabitant of the intestinal canal, are harmless under ordinary circumstances. In conditions of injury to the intestinal mucosa these organisms become virulent (Fermi and Salto). Other organisms, like the *B. putrificus*, the *B. aërogenes capsulatus*, which are obligatory anaërobes, thrive in the colon when there is no oxygen (Herter) and break up protein into the carbocyclic, toxic substances.

It was demonstrated by Baumann that these split products are very toxic, but that when they are united with sulphuric acid they have lost their poisonous effect. Baumann found that phenol sulphate is a normal urinary constituent and that the administration of phenol increases the elimination of phenol sulphate in the urine. Baumann and Herter reported that not only phenol, but also other substances were excreted in the urine as conjugated sulphates. They also observed that phenol unites not only with sulphuric acid but also with other radicals. This was confirmed by Schmiedeberg, who found that phenol unites with glycuronic acid. Upon poisoning dogs with phenol, Baumann found that the liver became rich in phenol sulphates. For example, in 100 parts of liver he found nineteen times as much tribromphenol as in 100 parts of blood. This observation seemed to prove that the liver is the seat of conjugation of phenolic and indolic radicals with sulphuric acid. The results of other scientists were, however, contradictory, as will be seen from the following references:

Lang determined the quantity of ethereal sulphates in the urine of geese before and after extirpation of the liver. Though his analytical differences are rather small, and should not be taken conclusively, still he was led to believe that the synthesis of the ethereal sulphates was not exclusively performed in the liver.

In experiments performed *in vitro* Kochs also demonstrated, so it appeared to him, that the liver was not the only seat of sulphoconjugation. He took portions of liver, kidney, pancreas, thymus, muscles, and minced each organ respectively and added phenol and disodium sulphate. He kept these mixtures at body temperature or else at 8° to 12° C. He reported that all the tissues save the thymus took part in the synthesis. He obtained the same results with ortho-, meta-, and para-dioxyphenol.

Landi repeated the experiments of Kochs, using, however, only liver tissue. But, as he says, due to the fact that the decomposition sets in so very soon, he could not confirm Kochs' findings. In order to throw more light on the subject he made perfusion experiments with the liver, and he came to the final conclusion that the seat of conjugation of the phenolic and sulphuric acid radicals was not the liver but the intestines.

The observations of Landi found no confirmation and were directly contradicted by the results of Embden and Glaessner. They performed perfusion experiments on the organs of dogs, using the liver, kidneys, muscle, lungs, and small intestines. From their investigations they concluded that the liver was the most important organ for the formation of the ethereal sulphates. Smaller quantities of ethereal sulphates are produced in the lungs and the kidneys, but the muscle tissue and the small intestine play a very insignificant role in the production of the ethereal sulphates. Reale, from his observations, was firmly convinced that the liver was the seat of the synthesis of the conjugated ethereal sulphates.



In normal conditions of the alimentary tract, Strauss and Philipsohn found no phenol in the urine of human beings, and they concluded that under normal conditions the phenol and other radicals were conjugated with sulphuric acid. According to these authors the liver is the seat of this conjugation.

Herter and Wakeman took 7 grams of liver, kidney, muscle, brain, and blood respectively, which they minced, and treated each tissue with 10 c.c. of a weak phenol solution, and allowed to stand for two to three hours. The mixtures were then distilled, and they found that there was a loss in the phenol distilled over. The liver retained most of the phenol, then came in order the kidneys, muscle, and brain.

In hepatic disease there have been observed disturbances in the elimination of the ethereal sulphates. In conditions of jaundice Biernacki found four times as much ethereal sulphates as normally. Darenberg and Perroy found an increased excretion of indol and skatol in the urine of jaundiced individuals. Labbe and Vitry obtained similar results. Magrageas obtained varying amounts of ethereal sulphates in icteric patients.

The question has been discussed by Eiger and Hopazde whether the aromatic compounds formed in the system are diminished in amount and destroyed under normal conditions of hepatic activity, and whether in cases of disturbances of the function of the liver, these compounds are obviously increased and placed at the disposal of the liver for conjugation with sulphuric acid. The subject is important in its relation to cases of disease of the hepatic parenchyma, more so than in cases of simple biliary stasis. The ethereal sulphuric acids are most frequently, both absolutely and relatively, increased in atrophic cirrhosis of the liver, and most markedly in tumors of the liver.

Finizio studied the excretion of ethereal sulphates in normal individuals, in a patient suffering with an echinococcus cyst of the liver, and in cases of hepatic cirrhosis. He found that when he administered thymol to the normal or echinococic individual there was a marked increase in the ethereal sulphate output in the urine, whereas the cirrhosis patient showed no such increase.

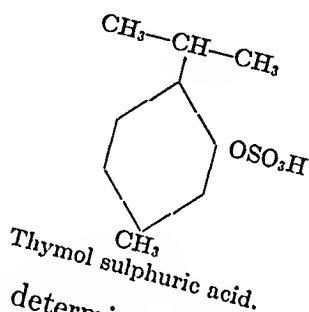
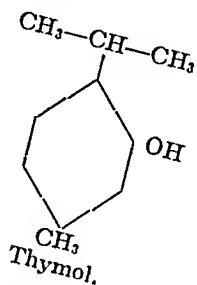
It has been quite definitely established that normally the inorganic sulphates of the urine form about 70 per cent. of the total sulphur and the remaining 30 per cent. are divided almost equally between the ethereal sulphates and the neutral sulphur.

It is, of course, impossible to rely upon the excretion of ethereal sulphates as an index of hepatic function. The proteins that are ingested daily give rise to their quota of aromatic radicals which influence the quantity of the conjugated sulphates excreted.

It has seemed to me advisable, therefore, to administer a definite quantity of an aryl compound and to examine the urine for the conjugated products of this substance. For the purposes of

this work thymol seems to be the most suitable aromatic substance to use.

Thymol is meta-isopropyl-cresol. Baumann and Herter have found that thymol sulphuric acid occurs in the urine of rabbits after thymol administration. Vogeliuss reported that the feeding of 0.5 gram thymol increases the output of ethereal sulphates from 0.05 gram to 0.107 gram per 100 c.c. of urine. Blum, Preusse and Finizio have separately reported that thymol is eliminated in the urine as thymol sulphuric acid and as thymol hydroquinone sulphuric acid.



I adopted the following technic for the determination of hepatic sufficiency by means of the ethereal sulphate output.

The patient received a dose of castor oil to clean out his bowels. He was then kept on a known diet for two days, during which time the urine was collected, preserved with a few drops of formaldehyde, and analyzed for total sulphur and ethereal sulphates.<sup>1</sup> On the third day the patient received a capsule containing 0.5 gram thymol. A dose of olive oil is administered to the patient several hours after the thymol dose in order to dissolve the thymol and increase its absorption from the intestinal canal. The urine was collected for the next forty-eight hours, preserved with a little formaldehyde and analyzed for total sulphur and ethereal sulphates.

If all the thymol were absorbed and if all the thymol were conjugated with sulphuric acid and none with glycuronic acid the 0.5 gram thymol would cause a marked increase in the percentage of the ethereal sulphates. If the liver were not functioning properly the thymol would not be conjugated and the percentage of ethereal sulphates would be only slightly different from what it had been on the first two days.

It is probable that each individual cell of the hepatic parenchyma takes part in all of the liver functions; it is possible, however, that different portions of the liver lobule may have specific functions. In the former case it is most likely that a reduction in the ability of the liver to perform one function will be accompanied by a proportional reduction in all the liver functions; in the latter case one or

<sup>1</sup> The total sulphur was analyzed by Benedict's method, and the ethereal sulphates by Folin's method.

more functions of the liver may be disturbed without affecting the other hepatic functions. One objection to the study of the function of any organ as an index of disease of that organ is that it is perhaps possible for the healthy portion of the diseased organ to compensate and assume the work of the whole gland. In such a condition, of course, the functional capacity of the organ may be normal and would be no index of the pathological changes in that organ. Under these circumstances only marked destructive changes would leave their impress on the functional sufficiency of the organ.

#### ETHEREAL SULPHATE ELIMINATION BEFORE AND AFTER THYMOL ADMINISTRATION.

Case No.	Diagnosis.	Total sulphur, gms.		Ethereal sulphate sulphur, gms.		Ethereal sulphate sulphur, per cent.	
		Before thymol.	After thymol.	Before thymol.	After thymol.	Before thymol.	After thymol.
1	Normal	2.0375	2.1295	0.2893	0.5646	14.2	26.8
2	Gastritis	1.9428	1.7427	0.1457	0.3380	7.5	19.4
3	Fracture	2.7467	2.5527	0.3131	0.6024	11.4	23.6
4	Congestion of liver	0.9852	0.0734	0.1753	0.7069	17.8	26.8
5	Congestion of liver	1.7345	1.6982	0.2480	0.3610	14.3	21.2
6	Gall-stones	2.7628	2.8075	0.7597	1.0303	27.5	36.7
7	Gall-stones	3.0042	2.6826	0.3965	0.8474	13.2	29.4
8	Cholecystitis	2.7807	2.6437	0.4866	0.7428	17.5	28.1
9	Atrophic cirrhosis	2.2328	2.3029	0.2791	0.3400	12.5	15.2
10	Tumor of liver	1.9492	1.8757	0.1637	0.3676	8.4	19.6
11	Cancer of liver	2.7526	2.6278	0.6083	0.6648	22.1	25.3
12	Syphilis of liver	2.8104	2.9075	0.3990	0.5437	14.2	18.7

The results that we have obtained in the cases cited in the accompanying table are very encouraging. The work is now in progress. We are collecting comparative data as to the positive incidence of this test and other tests of liver sufficiency in the same case of hepatic disease.

#### SOME CLINICAL AND EXPERIMENTAL OBSERVATIONS ON GASTRIC ACIDITY USE OF THE GAS-CHAIN METHOD.

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CHICAGO.

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IN order to determine the effect produced by chronic inflammatory and altered physiological changes in the gastro-intestinal tract, I have undertaken the study of the gastric secretion in such conditions by means of the exact gas-chain method of determining the acidity and have plotted curves, comparing the results with those gained by

the titration method. Previous to this time acidity curves have been made clinically only by the titration method. My estimations were made from specimens collected at short intervals after test meals in clinical cases and in animal experiments. In order to obtain pure juice in the latter experiments Pawlow pouches were made and estimations of secretion carried on before and after the production of lesions or altered physiological conditions. In such surgical conditions there may be an increased acidity in the stomach contents; in these observations I have attempted to determine whether such an increase is due to an actual increased acidity in the gastric juice.

The apparatus used in the gas-chain method of determining the hydrogen ion concentration was put at my disposal by J. F. McClendon.<sup>1</sup> This apparatus consists of a hydrogen electrode, a calomel electrode and a potentiometer for measuring electromotive force. The principle of the gas-chain method is well described by Sedgwick.<sup>2</sup> As to the colorimetric determination of the hydrogen ion concentration the results so far, when applied to gastric contents containing varying amounts of protein and salts, have proved inaccurate and unavailable for following changes in reaction during digestion.

A solution is acid in reaction when it contains an excess of hydrogen over hydroxyl ions, neutral when they are in equal numbers and alkaline when hydroxyl ions predominate. Pure distilled water dissociates into hydrogen and hydroxyl ions, the extent of the dissociation being such that in one liter of water at 22° C. there is approximately  $\frac{1}{100000000}$  gram of hydrogen ions; that is, concentration of the hydrogen ions is  $\frac{1}{100000000}$  normal (atomic weight of hydrogen as 1). The shorter method of representing so many figures is usually adopted, the logarithmic notation: thus,  $\frac{1}{100000000}$  H. Acid =  $10^{-7}$  or simply pH 7. Since there is one hydroxyl ion formed for each hydrogen ion the concentration of the hydroxyl ions must also equal pH 7.

The measurement of the pure gastric juice has been made by Menten,<sup>3</sup> and found to vary from pH = 0.92 to 1.58, highest in the appetite juice and lowest in the secretion in the empty stomach. Michaelis and Davidsohn<sup>4</sup> state that the average acidity of the stomach contents after an Ewald test meal means 0.028 to 0.0015; hyperacidity, 0.011 to 0.088; hypoacidity, 0.000,0041 to 0.000,0001. McClendon,<sup>5</sup> after normal meals, found a rise in acidity for two or

<sup>1</sup> Hydrogen and Hydroxyl Ion Concentration in Physiology and Medicine, Med. Rev. of Rev., 1916, xxii, 333.

<sup>2</sup> Hydrogen Ion Concentration of the Gastric and Duodenal Contents in Children, Tr. Am. Pediat. Soc., May, 1915.

<sup>3</sup> Acidity of Undiluted Normal Gastric Juice from a Case of Human Gastric Fistula, Jour. Biol. Chem., 1915, xxii, 341-343.

<sup>4</sup> Die Bedeutung und die Messung der Magensaftacidität, Ztschr. f. Exper. Path. u. Therap., 1910-1911, viii, 398.

<sup>5</sup> Acidity Curves in the Stomachs and Duodenums of Adults and Infants Plotted with the Aid of Improved Methods of Measuring Hydrogen Ion Concentration, Am. Jour. Physiol., 1914, xxxv, 191-199.

three hours, when it remained constant until the food had left the stomach. Carlson<sup>6</sup> believes that the view of Pawlow<sup>7</sup> that gastric juice is secreted at uniform and constant acidity is true for man only in regard to the appetite, digestive and hunger juice secreted at a fairly high rate, and has observed that the normal gastric mucosa is capable of secreting a juice of submaximal acidity. Hardt<sup>8</sup> after experimental production of gastric and duodenal ulcers found no increased acidity. Grey<sup>9</sup> after cholecystogastrostomy found no change in the acidity of the gastric secretions.

Pawlow believes that the slower rate of secretion may give a chance for the HCl acid to be partly neutralized by the mucus in the stomach. Boldyreff<sup>10</sup> has shown the entrance of the intestinal contents to be the most important factor in neutralization of the stomach contents.

For the purpose of comparison of acidity estimations a standard test meal was adopted which consisted of two slices of bread with crusts removed and two glasses of distilled water. In all estimations the Rehfuß<sup>11</sup> tube was used for collecting specimens. Collections were made every fifteen minutes from the time the test meal was eaten until no more material could be aspirated. Unfiltered gastric juice was used in the estimations, though at times it was strained through coarse gauze. In order to compare the actual acidity to the acidity obtained by the usual titration methods, samples of the juice were titrated against a  $\frac{N}{50}$  KOH solution, using dimethyl amino azobenzene and phenolphthalein as indicators. I have found that the value of these indicators used clinically in determining free and total acidity by titration with an alkali is in many cases parallel, though not equivalent, to the actual acidity as determined by the gas-chain method (Fig. 1). Much discussion has arisen as regards the value of the titration methods; consequently, I have made observations by both methods, and have plotted, also, corresponding curves to compare the values of the dimethyl amino azobenzene acidity to the actual acidity. Fig. 1 shows the curves running fairly constantly parallel throughout; however, the acidity as determined by the "indicator method" is uniformly higher than the actual acidity. Fig. 2 shows the plate for determining the hydrogen ion concentration from the dimethyl and phenolphthalein acidity as

<sup>6</sup> The Secretion of Gastric Juice in Man, *Am. Jour. Physiol.*, 1915, xxxvii, 51. A Note on the Chemistry of Normal Human Gastric Juice, *Am. Jour. Physiol.*, 1915, xxxviii, 248.

<sup>7</sup> The Work of the Digestive Glands, 1910, translated by Thompson.

<sup>8</sup> The Secretion of Gastric Juice in Cases of Gastric and Duodenal Ulcers, *Am. Jour. Physiol.*, 1916, xl, 314.

<sup>9</sup> *Jour. Exper. Med.*, 1916, xxiii, 15.

<sup>10</sup> Self-regulation of Acidity of Gastric Contents and Real Acidity of Gastric Juice, *Quarterly Jour. Exper. Physiol.*, 1914, vii, 1-12.

<sup>11</sup> A New Method of Gastric Testing, with a Description of a Method for Fractional Testing of Gastric Juice, *AM. JOUR. MED. SC.*, 1914, cxlvii, 848.

determined with the above indicators. This assumes the acidity to be in terms of pure HCl acid, which dissociates, as shown by the

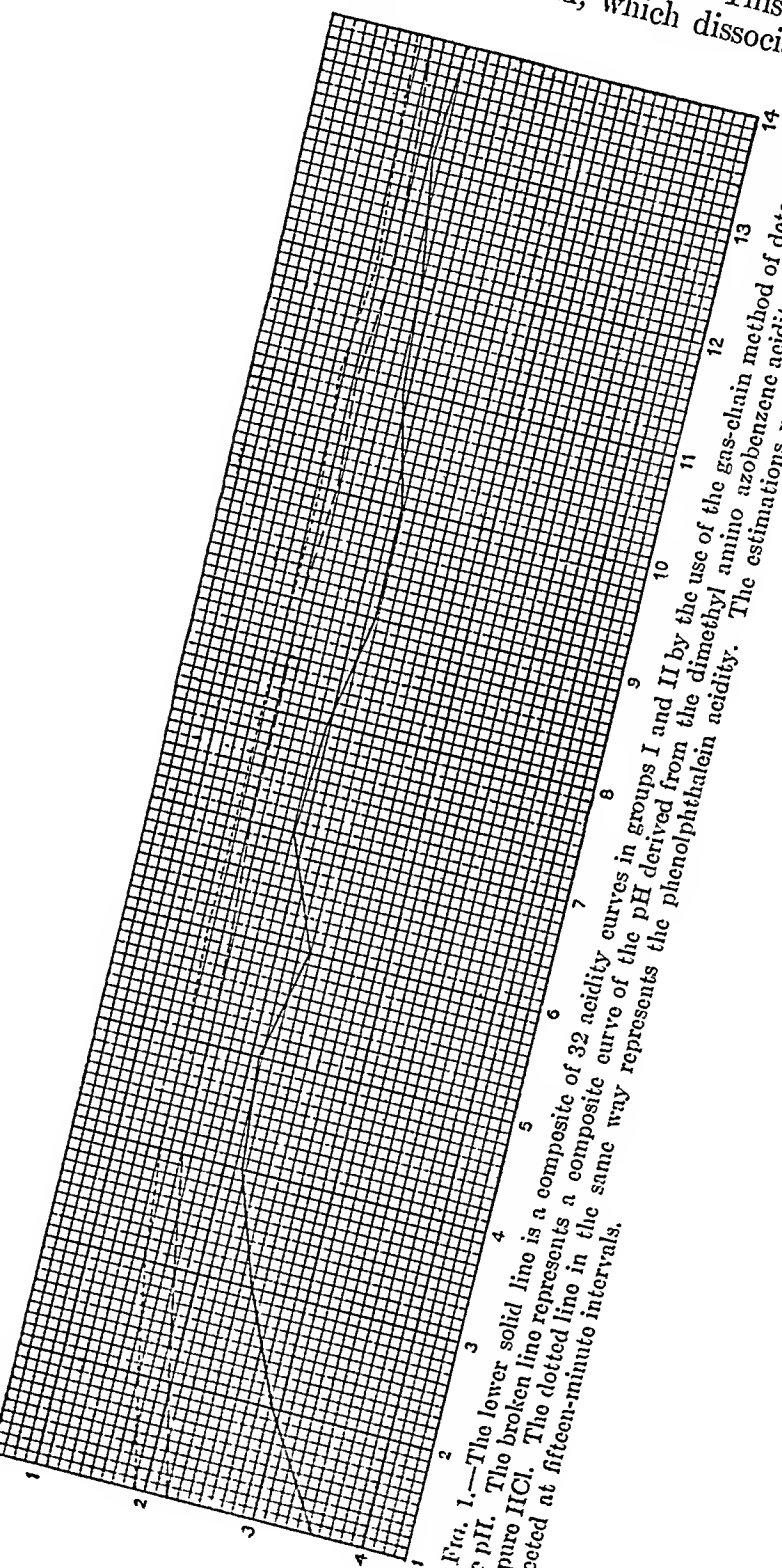


FIG. 1.—The lower solid line is a composite of 32 acidity curves in groups I and II by the use of the gas-chain method of determining the pH. The broken line represents a composite curve of the pH derived from the dimethyl amino azobenzene acidity, assuming it to be pure HCl. The dotted line in the same way represents the phenolphthalein acidity. The estimations were made from specimens collected at fifteen-minute intervals.

curve. Fraenkel<sup>12</sup> found the Congo-red acidity to be almost constantly parallel to the actual acidity as determined by the gas-chain method, and states that the phenolphthalein acidity does not show the free HCl acid even in the pure gastric juice.

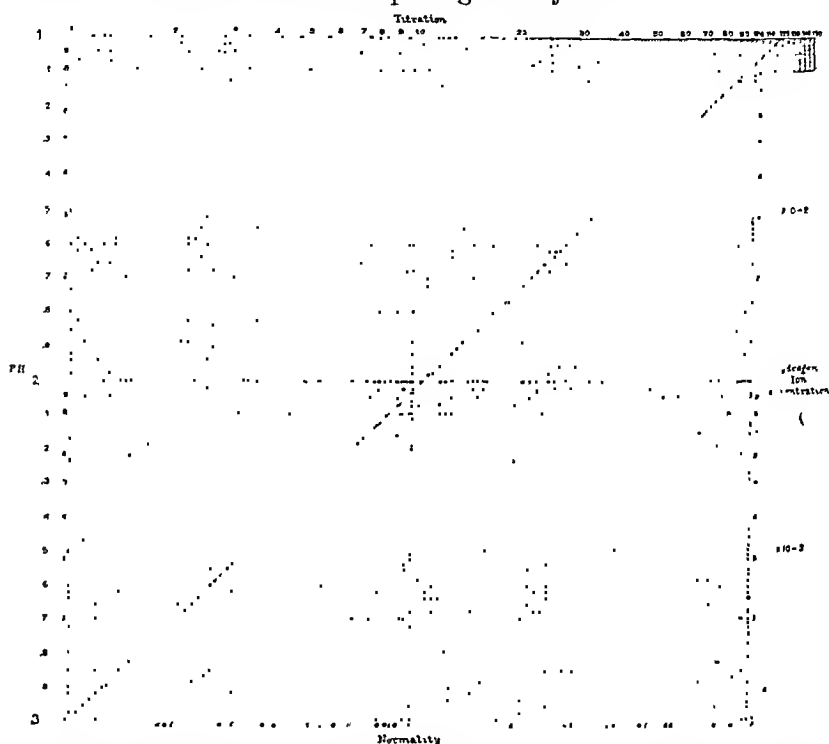


FIG. 2.—By this chart the degree of dissociation of HCl at different degrees of strength may be determined and either the hydrogen ion concentration or the pH estimated. The curve continued from 120 c.c. N/10 HCl = pH 1 would show the dissociation of HCl at higher concentrations. 130 c.c. N/10 HCl = pH 0.996; 140 c.c. N/10 HCl = pH 0.993; 150 c.c. N/10 HCl = pH 0.9. (Chart plotted for me by J. F. McClendon.)

The plotted curve of acidity of 37 cases may be divided into several phases for study: (1) the ascension, usually the first hour, indicating the rapidity and intensity to a known stimulus; (2) the high point or acme, to note whether accelerated or retarded and whether abrupt or sustained; (3) the period of descent or decline and the possible secondary rise, also to note the character and modification of the food residues. The cases observed include chronic appendix and gall-bladder cases, before and after operation, hernia, carcinoma of the stomach, kidney stone, huge ovarian cyst, gastrojejunostomy, duodenal ulcer, prostatic hypertrophy and a few remote surgical conditions.

In Group I, 10 of 13 cases tend to a gradual rise, and at the end of the first hour have reached the maximum from which they usually

<sup>12</sup> Die Wasserstoff-Ionenkonzentration des reinen Magensaften und ihre Beziehungen zur elektrischen Leitfähigkeit und zur titrimetrischen Acidität., *Ztschr. Exper. Path. u. Therap.*, i, 431, 1995.

decline gradually. Three cases have a delayed rise. The average time juice could be obtained was two and a half hours, food being absent in the last fifteen minutes to three-quarters of an hour.

In Group II the curve either remains continuously high, or after a fall, undergoes a second rise, often higher than the primary one, near or at the end of digestion. In this first subdivision are 6 cases, 2 of which have a delayed rise; in the second subdivision are 12 cases, 1 having a delayed rise. The average time specimens could be obtained in the first division of Group II was two hours; in the second, two and three-quarter hours; in one-half of these cases food was present to the end.

In Group III, I have placed 5 cases of hypoacidity in which the acidity was less than  $\text{pH} = 4$ . Michaelis and Davidsohn place hypoacidity between 0.00041 and 0.0000001. Considerable peptic digestion takes place at  $\text{pH} = 4$  and very rapid digestion at  $\text{pH} = 0.78$  (Sorensen<sup>1</sup>), so that digestion is retarded but not stopped until acidity is less than  $\text{pH} = 4$ . Dimethyl amino azobenzene does not react to an acidity later, after removal of a gall-bladder with stones, the curve of acidity later, after removal of a gall-bladder with stones, rose to a normal acidity curve. The average time specimens could be obtained in this group was two and three-quarter hours.

Hypersecretion was demonstrated in gastric ulcer cases thirty years ago (Rubow). Recently it has been found not only in inflammatory conditions of the gall-bladder, appendix and in pelvic and other organs but in normal individuals. The vagus is considered one factor in producing this condition.

The values of  $\text{pH}$  before operation were taken in 8 cases with chronic appendicitis and a composite curve plotted (Fig. 3). The curve gradually rises to the end of the first one and a half hours, then falls slightly to the two-and-a-half-hour period, when it begins a secondary rise higher than the digestive rise, lasting to the end of collection. Two of these cases, having definite gastric disturbances, had early high acidity with an exaggerated secondary rise. Secretion in these chronic appendix cases was obtained for an average of two and three-quarter hours, but was obtained longer in the 2 cases with definite gastric symptoms. Food was present in 3 cases without symptoms to the end of observation, but in the others it was absent in the last three-quarters of an hour.

In addition to cases studied by the fractional method I ran a series of 14 clinical cases, comparing the secretion obtained one hour after an Ewald meal before and after operation for chronic appendicitis. I estimated the titration acidity in all of these cases, the total chlorides in 5 and determined the  $\text{pH}$  in 9 cases. There was some variation in the  $\text{pH}$  but no constant change after operation; therefore these results are not tabulated. A composite curve of 7 cases of gall-bladder disease was plotted (Fig. 3). On account of variations in the individual acidity an irregular curve was formed. The curve rises rather suddenly in the



first three-quarter hour, then falls in an irregular wave to the two and a fourth hour period, when it begins its secondary rise higher than the digestive rise and retains it to the end of collection. Secretion was obtained in these cases an average of only a little over two

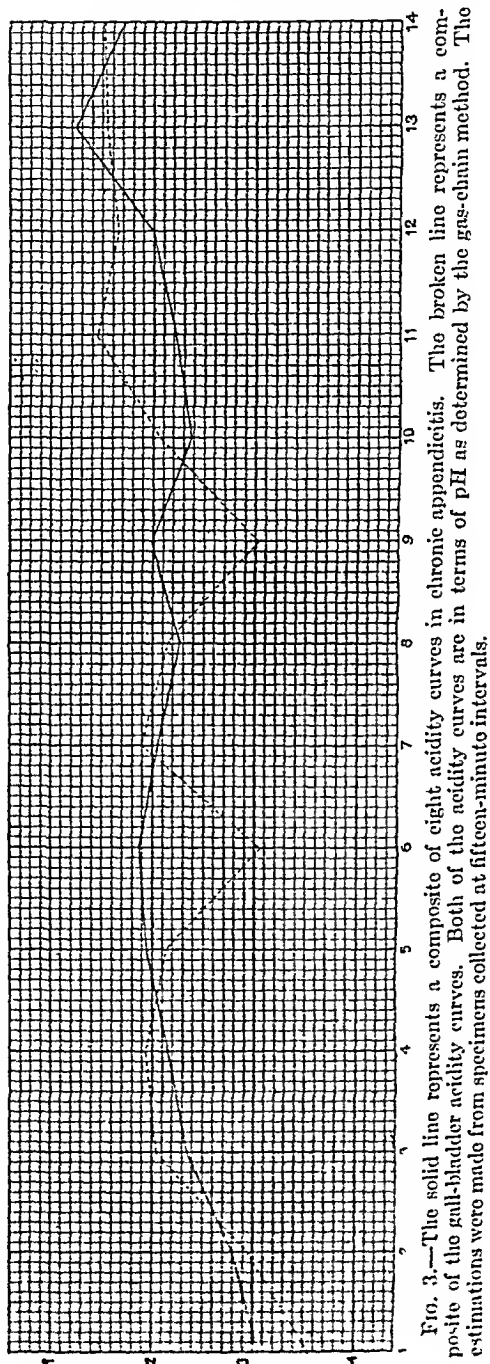


FIG. 3.—The solid line represents a composite of eight acidity curves in chronic appendicitis. The broken line represents a composite of the gull-bladder acidity curves. Both of the acidity curves are in terms of pH as determined by the gas-chain method. The estimations were made from specimens collected at fifteen-minute intervals.

hours as compared to two and three-quarter hours in chronic appendix cases. Food was present in all of the specimens of secretion in only 1 case, in the others it was absent in the last fifteen minutes to three-quarter hour, while in the chronic appendix cases, though secretion was obtained three-quarters of an hour longer, food was present in 3 cases in all of the specimens. A two-year gastrojejunostomy is interesting from the high actual acidity with a secondary rise at the end, and the length of time secretion was obtained, three and a half hours. This rather increased length of time corresponds to other observations.

The gastric symptoms in chronic appendicitis may be caused primarily by a reflex spasm of the pylorus with secondary changes in secretion and acidity (Aaron,<sup>13</sup> or, according to Fenwick<sup>14</sup> and McGuire,<sup>15</sup> the gastric secretions may be changed primarily, with the other changes secondary to the irritation of a hyperacidity. Fenwick believes the constant excess of free HCl gives rise to a spasmodic closure of the pylorus and also excites a violent gastritis with often interstitial hemorrhages. He believes that 12 per cent. of the cases of hypersecretion are due to disease of the appendix and that there is usually an increase both in quantity and acidity, when active irritation of the appendix is present. Paterson<sup>16</sup> says that the appendix influences the gastric secretion but thinks it due to intestinal stasis rather than pyloric spasm. Ochsner<sup>17</sup> says that there is undoubtedly a contraction of the ileocecal valve during an acute exacerbation of appendicitis. This in turn may give rise to a contraction of the duodenal and pyloric sphincter and in this way the normal passage of food from the stomach is impaired. Long and short, or local, reflex nerve paths to the stomach from the appendix and intestine have been demonstrated clinically and experimentally.<sup>18</sup>

<sup>13</sup> Chronic Appendicitis, Pylorospasm and Duodenal Ulcer, a Preliminary Note, Jour. Am. Med. Assn., 1915, lxiv, 1845.

<sup>14</sup> The Clinical Significance of Gastric Hypersecretion and its Connection with Latent Disease of the Appendix, Proc. Royal Soc. of Med., 1910, iii, 3, 177.

<sup>15</sup> Tr. South. Surg. and Gynec. Assn., 1911, xxiii.

<sup>16</sup> Appendicular Gastralgia, or the Appendix as a Cause of Gastric Symptoms, Proc. of Royal Soc. Med., 1910, iii, 3, 187.

<sup>17</sup> Further Observations on the Anatomy of the Duodenum, Am. Jour. Med. Sc., 1906, cxxxii, 1.

<sup>18</sup> Opitz: Quoted by Kenefick, Med. Rec., 1915, lxxxviii, 355.

Cannon, W. B.: The Mechanical Factors of Digestion, 1911.

Cannon, W. B.: The Acid Control of the Pylorus, Am. Jour. Physiol., 1907, xx, 301.

Carlson, A. J.: Reflexes from the Intestinal Mucosa of the Stomach, Am. Jour. Physiol., 1914-1915, xxxvi, 191.

Alvarez, W. C.: The Motor Functions of the Intestine from a New Point of View, Jour. Am. Med. Assn., 1915, lkv, 388-394.

Irritability in Different Parts of the Stomach, 1916, xli, 321.

Keith, A.: An Account of Six Specimens of the Great Bowel Removed by Operation with Some Observations on the Motor Mechanism of the Colon, Brit. Jour. Surg., 1914-1915, ii, 576-599.

A New Theory of the Causation of Enterostasis, Lancet, London, 1915, ii, 371-375.

Barclay, A. E.: Radiological Studies of the Large Intestine, Brit. Jour. Surg., 1914-1915, ii, 638-652.

In my experimental observations I used the Pawlow pouch in order to obtain pure juice and found it of value in controlling operative and postoperative hemorrhage to run a buttonhole suture around the incised stomach wall before invagination. In order to lessen the tendency to breaking down of the mucosa between the main stomach and the pouch I invaginated the cut mucosa and submucosa as Keeton<sup>19</sup> has suggested, not so that the closed edges of the two stomachs fell against each other, but so that they formed a cross

C  
E.....A + B (Fig. 4).  
D

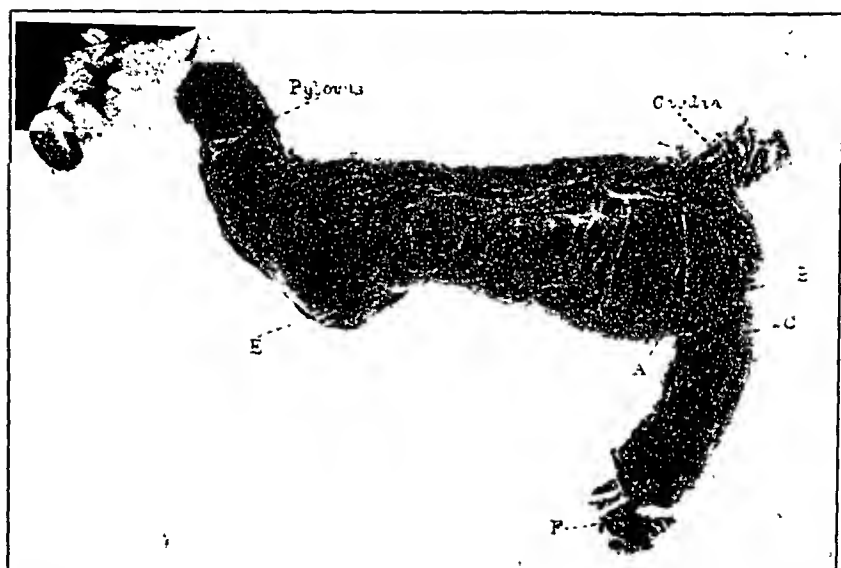


FIG. 4.—Photograph of Pawlow stomach in Exp. 5. Line *E-A* is the line of the incision through the stomach wall. From *A* to *B* the mucosa and submucosa have been cut and peeled back from the muscle after which the ends are invaginated along the line *A-B* and in the small stomach at right angles, *C* to *D*. The point *D* is located on the posterior wall opposite *C*. The pouch is completed by invaginating the stomach wall from *A* to *F*, leaving the small opening at *F*. The incision through the main stomach is completely closed from *A* to *E*.

In my experiments on dogs, lesions similar to chronic appendicitis with adhesions in the human were attempted. The cecum of the dog forms a rather long spirally twisted appendix. A stenosis of this cecum and adhesions to the colon, ileum and abdominal wall were produced.

#### ANIMAL EXPERIMENTS.

1. Pawlow pouch, January 17, 1917. Lesions of cecum, January 24, 1917. Slightly inflamed cecum removed and adhesions freed, January 29, 1917. Posterior gastrojejunostomy, March 5, 1917.

<sup>19</sup> *Am. Jour. Physiology*, 1914, xxxiii, 25

Chloroformed, May 28, 1917. Gastro-enterostomy and Pawlow pouch results good.

2. Pawlow pouch, February 23, 1916. Collections. Lesions of cecum, April 10, 1916. Posterior gastrojejunostomy, May 8, 1916. Collections. Dog chloroformed, August 4, 1916. Necropsy: adhesions of cecum to colon, ileum and abdominal wall. Gastrojejunostomy opening patent.

3. Pawlow pouch, March 2, 1916. Lesions of cecum, March 27, 1916. Chloroformed, April 2, 1917. Wound infection. Definite inflammation of cecum.

4. Pawlow pouch, October 20, 1916. After collections, lesions of cecum, November 20, 1916. Collections. Reoperated. Chloroformed, November 25, 1916. Necropsy: acute inflammation of cecum and peritonitis.

5. Pawlow pouch, November 27, 1916. Collections. Lesion of cecum, December 13, 1916. Inflamed cecum removed, December 28, 1916, adhesions to ileum, colon and abdominal wall freed. Chloroformed, January 13, 1917.

6. Pawlow pouch, December 1, 1916. Collections made similarly to experiment 5 as a normal control.

7. Pawlow pouch, January 2, 1917. Lesions of cecum, January 12, 1917. Distemper. Chloroformed, January 20, 1917. Necropsy: adhesions and stenosis of cecum.

8. Pawlow pouch, January 5, 1917. Lesions of cecum, January 15, 1917. Cecum removed and adhesions freed, January 20, 1917. Chloroformed, February 28, 1917. Necropsy: small communication between the two stomachs. Ulcer at suture line.

9. Pawlow pouch, January 16, 1917. Lesions of cecum, January 24, 1917. Acutely inflamed cecum removed. Peritonitis. Chloroformed, January 30, 1917.

10. Pawlow pouch, January 19, 1917. Lesions of cecum, January 26, 1917. Collections. Cecum removed, January 29, 1917. Distemper. Chloroformed, February 13, 1917.

11. Pawlow pouch, November 24, 1916. Collections. Emaciation and vomiting. Chloroformed, December 13, 1916. Necropsy: marked hour-glass contraction of stomach. No other pathology.

The following contains animal experiments illustrative of my results, the first column under "pH," showing the acidity determined by the gas-chain method. Under "HCl" is placed the dimethyl amino azobenzene and under "Total" the phenolphthalein, acidity, determined by the titration method.

EXPERIMENT 1. One of four test meals from Pawlow stomach before lesions were produced. Test meal, 75 grams Hamburg and 2 grams peptone:

Hr.	pH.	HCl.	Total.	C.c.
1	1.19	94	106	6½
2	1.27	72	94	1½
3	3.43	0	54	1
4	....	...	...	½

After production of stenosis of cecum and adhesions. One of five test meals:

Hr.	pH.	HCl.	Total.	C.c.
1	1.18	100	110	2½
2	1.18	90	104	1½
3	1.30	62	82	1
4	....	...	...	½

After removing cecum and freeing adhesions. One of seven test meals, one to twenty-three days after operation:

Hr.	pH.	HCl.	Total.	C.c.
1	1.22	98	119	3
2	1.23	96	110	2½
3	....	66	82	2
4	....	...	...	1

One typical test meal from five tests, four to seventeen days after a gastrojejunostomy:

Hr.	pH.	HCl.	Total.	C.c.
1	1.08	84	98	5
2	1.06	102	114	6
3.4	1.01	106	118	8
5	1.03	98	110	4
6	1.01	100	112	2

EXPERIMENT 5. Four test meals made from Pawlow stomach. Illustrative meal after 75 grams Hamburg and 2 grams peptone:

Hr.	pH.	HCl.	Total.	C.c.
Continuous secretion	1.43	42	48	1
1	1.28	60	66	4
2	1.32	60	66	5
3	1.33	68	74	3½
4	1.60	80	86	3
5	1.52	54	60	3
6	1.50	64	68	2½
7	1.26	64	68	2
8	1.43	42	60	1½

After production of stenosis of cecum and adhesions. One of two test meals:

Hr.	pH.	HCl.	Total.	C.c.
Continuous secretion	1.35	78	86	4
1	1.20	74	84	20
2	1.20	64	72	14
3	1.15	90	100	10
4	1.14	84	88	8
5	1.33	82	88	8
6	1.36	80	82	7
7	1.25	80	88	10
8	1.26	76	82	9
9	1.52	80	86	6

Twelve days after removal of inflamed cecum. No appetite. Test meal given by tube:

Hr.	pH.	HCl.	Total.	C.c.
Continuous secretion	1.10	101	116	3
1	1.30	94	104	2½
2	1.30	98	106	3

EXPERIMENT 8. Average of five test meals from Pawlow stomach. Test meal, 75 grams Hamburg and 2 grams peptone:

Hr.	pH.	HCl.	Total.	C.c.
1	1.25	85	105	4½
2	1.18	92	109	6½
3	1.22	70	80	2
4	1.49	80	95	1½
5	1.65	50	78	2
6	1.18	95	103	1
7	1.20	92	100	1

After production of stenosis and adhesions of cecum. Average of four test meals:

Hr.	pH.	HCl.	Total.	C.c.
1	1.23	74	85	7
2	1.16	86	96	5
3	1.16	62	87	4½
4	1.18	74	89	1½
5	....	28	54	½
6	....	24	48	½

After removal of long cecum. Average of five test meals:

Hr.	pH.	HCl.	Total.	C.c.
1	1.17	116	128	8
2	1.15	121	133	10½
3	1.16	113	125	5½
4	1.16	90	106	3
5	1.20	108	118	1
6	1.20	108	118	1

EXPERIMENT 10. Average of three test meals from Pawlow stomach. Test meal, 75 grams Hamburg and 2 grams peptone:

Hr.	pH.	HCl.	Total.	C.c.
1	1.26	89	104	3
2	1.22	74	94	1½
3	....	...	...	½
4	1.4	72	96	½

After production of stenosis of cecum and adhesions. Average of three test meals:

Hr.	pH.	HCl.	Total.	C.c.
1	1.14	102	116	4
2	1.13	107	122	1½
3	1.27	100	110	1
4	1.18	100	109	1
5	1.18	100	108	1

After removal of cecum and freeing of adhesions. Average of five test meals:

Hr.	pH.	HCl.	Total.	C.c.
1	1.12	118	130	3
2	1.14	116	124	4
3	1.12	116	119	1½
4	1.14	110	114	1
5	1.14	110	112	½

**RESULTS OF EXPERIMENTS.** In considering the results of the animal experiments, there was a definite increase in secretion in nearly one-half of the cases after lesions of the cecum were produced. In 1 case there was also an increase in continuous secretion; in the others there was a hypersecretion with a slightly longer period of flow. After removal of the "cecum" there was also a marked increase in quantity in 1 case and slight increase in another. The actual acidity after the lesions, as well as after the removal of the "cecum," was slightly higher than that ordinarily found corresponding to an increased flow of secretion. After gastrojejunostomy (Experiments 1 and 2) there was a decided increase in the rate of secretion in both cases as well as a prolonged flow of juice in 1 case. The acidity was slightly increased after gastrojejunostomy, associated with a more rapid rate of flow. After hour-glass contraction of the stomach in 3 cases there was no decrease of acidity, although frequently a decrease in such cases has been found clinically. There was a slightly increased rate of flow in some instances, in others a decreased rate, associated with emaciation and vomiting. One case, Experiment 11, is listed.

**SUMMARY OF CLINICAL AND EXPERIMENTAL WORK.** In a group of surgical cases, it has been shown that the curve of acidity may rise higher at the end of digestion than it has during the digestive rise. After certain surgical lesions have been made upon the gastrointestinal tract of animals, it is demonstrated that there is a slight increase in acidity in the secreted gastric juice; in some reflex manner, however, lesions of the cecum or other changes may cause an increased rate of flow. There must be some disturbance of the factors concerned in neutralization of the acidity associated with the factors controlling the discharge of chyme through the pylorus. The contour of the curve of acidity must be influenced by the food and fluids present, the intensity and duration of the appetite and food secretion, the emptying time of the stomach, the regurgitation of alkaline and duodenal contents, the gastric mucus and the saliva.

**CONCLUSIONS.** 1. The clinical study of the gastric secretion must be done by examination of specimens taken at short intervals during digestion. Examination of a single specimen for comparative purposes is inexact and inadequate.

2. There is often a persisting high acid secretion after the digestive period. The digestive acidity may fall with a secondary late rise. Frequently surgical cases have this type of curve.

3. Clinically, the pH derived from the titration method is uniformly higher than the actual acidity as determined by the gas-chain method.

4. In animal experiments, after production of chronic inflammation of the long appendix of the cecum, with adhesions, after the removal of this appendix, after gastrojejunostomy and hour-glass stomach, no definite increase in actual acidity of pure gastric

juice was observed. There was an increased rate of flow and a prolonged flow in some cases.

5. The presence of increased acidity in the stomach contents in these surgical conditions must therefore be explained by factors noted in the summary above and not to an actual increased acidity of the gastric juice.

## NOTES ON THE PROGNOSTIC VALUE OF PSYCHOMETRIC TESTS AS COMPARED WITH CLINICAL SIGNS IN EPILEPSY.<sup>1</sup>

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From data now at hand it is obvious that the diagnosis and prognosis of many cases of essential epilepsy rest in no small degree upon accurate analysis of the so-called mental stigma of the disorder, the epileptic constitution, as well as the modifiability of the latter under appropriate training treatment. Likewise the course of the disorder is to be judged by the presence or absence of deterioration and its degree.<sup>2</sup> As regards deterioration, in the past we have been content for the most part to indicate it purely on the basis of a clinical estimate of behavior, ability to do work and like data. However, it now seems opportune for us to call to our aid a more precise method to determine the initiation of deterioration not only for prognostic reasons but also that one may early determine the efficacy of any definite plan of training treatment. The psychometric work of Eberschweiler and Jung and, more especially, the proofing test of Hahn, are suggestions in point. Although a large number of studies of this psychological character has appeared, Hahn<sup>3</sup> was able, in 1913, to check up some of his work on the same clinical material studied in 1903 and 1908. The time interval between the two sets of studies were from two to four years. As is natural the findings in his studies had to exclude the mental infirmity due simply to an arrest in growth and development as well as a proper allowance made for the wide variations of the primary endowment in such individuals. Hahn employed a

<sup>1</sup> Delivered as a part of the Symposium on Epilepsy and Allied States, Randall's Island, June 4, 1917.

<sup>2</sup> Clark: Clinical Studies in Epilepsy, Psychiatric Bull., January, 1916, to January, 1917.

<sup>3</sup> Association Studies in Youthful Epileptics, Archiv f. Psychiatric, 1913 lii, 1078.



very free and modifiable system of testing. In brief, he found the following in 7 cases studied:

The first case of medium deterioration showed an increase in tendency to revert to the child type of reaction (increase of deterioration). In the second case of mild deterioration he found the reaction time became prolonged in the later tests and there was a tendency to greater perseveration; clinically the case was supposed not to have increased in deterioration. In the third case the clinical and the psychological deterioration were quite in accord in spite of a cessation of attacks; there had never been many attacks in the case, and none since trephining a year before the final testing. Hahn's comment coincides with that of many other observers, clearly set forth by MacCurdy<sup>4</sup> in his epileptic deterioration study. Hahn says: "The psychic alteration in epileptics cannot therefore be straightway due to the convulsions, either to their number or severity, and an avoidance of attacks, however valuable practically, in most cases does not indicate a 'therapia magna.'" The fourth case studied was a child, aged thirteen years, at time of report, who showed deterioration in association with normal development. In the tests at two-year intervals the latest showed a prolongation of reaction time and a marked tendency to perseveration (signs of deterioration). It was interesting to note that the mental regression in nowise seemed to retard any phase of the physical growth. The fifth case was one of slight deterioration in a woman, aged thirty-three years. The tests showed practically no increased deterioration in spite of the fact that the woman had had severe attacks rather frequently since early childhood. It seemed possible, from the favorable testing (in 1904), that this woman might finally recover. The latest report (1908) showed that this outcome might still be expected. The sixth case, a woman, who had had no attacks from the first to the last test in a period of two years, showed steady and apparently normal development. The reaction time gradually approximated the normal and perseveration disappeared. In 1906 the psychological test was in accord with the clinical opinion that the case was a good example of "arrest," which was in sharp contrast to Case III, who also ceased having attacks but continued to deteriorate. Case VII, a woman, aged thirty-seven years, showed psychological accord with the clinical record of progressive improvement; the former even outran the prognostic acumen of the clinical recognition of the betterment.

There can be no doubt that a psychometric setting of epileptics would be eminently helpful to the diagnosis, prognosis and therapy of the disorder. Although the work may be fraught with much difficulty the study ought not to be neglected. At present the clinical criteria are too elusive and unsatisfactory to estimate the epileptic deterioration.

<sup>4</sup> A Clinical Study of Epileptic Deterioration, *Psychiatric Bulletin*, April, 1916.

As an earnest of the foregoing we have undertaken some repeated testings in a few epileptics at the Randall's Island institutions. The cases were selected at random for the purpose of noting the accordance or non-accordance of the changes in (1) convulsive frequency, (2) the clinical evidences of alterations in conduct, behavior and work, and (3) the more precise analysis of a psychological testing by the Binet, performance and simple word-association tests for recording the reaction time, perseveration and the range and flexibility in the intellectual and emotional life of the epileptic.

CASE I.—The first case is that of Harold E., who was admitted to the Randall's Island institutions April 21, 1916. He is now fourteen years old. He had an apparently normal development of childhood. The onset of his grand mal epilepsy at nine years of age seemed to have had little influence on his school work until the year preceding his admission, when he had to repeat one year. The attacks were reported to have occurred three or four weeks apart at that time. He has always possessed the character defects of the epileptic make-up, and these have become more pronounced during the past year.

Two years ago he Bineted 10.4, which was 1.6 years below his real age. During the examination it is recorded that he had a quiet demeanor; he was interested in everything in the room and talked in a straightforward manner, but his attention was very easily distracted. His reproductive memory was very good (six digits in figures and fifteen syllables). His general intelligence seemed normal. He had a normal grasp on the central idea of a story and laughed heartily over a humorous picture; he easily identified street scenes. He was rather unstable emotionally, and was reported to be quarrelsome at times. In 1915, when the first test was made, the attacks averaged one in three or four weeks, and were always grand mal in type, occurring at night. They continued through 1916 at about the same frequency. At present (1917) the frequency and severity of his epilepsy has apparently not undergone much change. However, his mental examination by the Binet test now shows him to be 8.2, two years less in the two-year interval since his first test. The whole test at present indicates considerable epileptic deterioration, there is a superficial reaction to word-association, and his time reaction is very much slowed; for instance, such words as book, storm and letter he takes thirty-five to forty seconds to respond. There is a marked tendency to perseveration, a clinging to the one type of word-response for a number of unrelated words given. His attitude during the test was marked by mannerisms. For instance, he sat with a dull, lethargic expression, his eyes shaded with his hand, and in an annoyed manner frequently held up his hand to the examiner and said, "Keep quiet," and "Do not say anything." Evidently he is aware of the slowness

and confusion of his thoughts and his difficulty in grasping the simple tests given him. His attitude, on the whole, was quite friendly throughout the examination, but he evidenced an abnormal reaction in shallowness of mental grasp and a rigidity in physical and mental response.

In this boy we find no apparent change in the number and severity of the epileptic attacks, but other clinical and psychological evidences show a relatively rapid progress in mental deterioration.

CASE II.—The next case is that of Elliot M., a man, now thirty-five years old. His birth was prolonged and instrumental. He did not talk until two years of age, and only formed full sentences when three years old. He began school at seven and discontinued at fourteen. He never reached the grammar grades, and often played truant. He often stole money as a boy, and drank, was passionate and of the typical epileptic. At twenty he had a right hemiplegia. A month after this stroke he had his first seizure. The attacks are mostly of the grand mal type. Two years ago, at the age of thirty-three, he Bineted 8.6 years. His performance test was fair but the reactions were slow and deliberate. His perception of form was good. His interest and attention were good. Perseveration was marked. While his coöperation on the test was good he required much encouragement. He was much embarrassed at not doing better at tests, not usually seen in ordinary essential epileptics. He had much difficulty in expressing himself, as he said, "The answers come to me and then leave me and I can't recall them."

He had three or four grand mal attacks a week the first three years. During the past five years the attacks have diminished in severity and frequency, and there now is a slight warning of a "rush of blood to the head." He is now able to lie down on the floor and unbutton his shirt before he becomes unconscious. His attacks now have diminished to about two a month instead of that many a week several years ago. His present mental examination, however, shows he Binets to 7.6 years of age mentally. He has lost a year in rating in the two years in spite of the diminution of epileptic attacks. It was found that while his attention was good throughout the test he thought more slowly and laboriously. His memory is badly impaired. He says he once read easily but cannot now recognize simple words. His reaction time is very slow; to such words as love, ship and door his time is over forty seconds. As this patient has a positive Wassermann in the spinal fluid his right hemiplegia is probably a specific thrombosis and his attacks are symptomatic or epileptiform.

The case is interesting because in spite of a great diminution of grand mal attacks the patient is deteriorating mentally, as shown by precise tests, although ordinary clinical evidence does not show this; that is, he is better behaved, does more consistent and good work

about the institution, and yet the underlying organic injury to the brain is probably progressive in character.

CASE III.—The next case, Mary D., is that of a woman, aged forty-six years, whose seizures began at puberty and continued for a few years, and occurred every other day. In spite of her epilepsy she was married at twenty-five and has one normal daughter, now seventeen years of age. Two years ago she Bineted 8.8 years. During the mental examination two years ago her demeanor was quiet. She had the general appearance of discouragement. Her memory for former and recent events was poor. Of ten pictures displayed in succession she was unable to recall any. She had poor mental grasp on stories and detailed descriptions. Her power of reasoning was poor and she was easily confused. She was having about fifteen seizures a month at the time of this examination. Her attacks apparently have not changed in frequency or severity since the testing two years ago.

Her present test shows her to be 7.6 years mentally, a loss of one year in two years. Her reaction time varies from two seconds to one minute and fifty seconds. In general the test showed great distractibility; she tried to talk of things that had no bearing on the tests. Her judgment and comprehension were poor and there was a great slowing in the reaction time.

On the whole the case showed deterioration of a mentality that also gave evidence of a defective primary endowment. In spite of the fact that there was no apparent change in the seizures in frequency or severity this patient is steadily deteriorating, and here the clinical and psychological tests are in accord if one excludes the consideration of the epileptic attacks which have undergone no change.

CASE IV.—The next case, Carrie H., is that of a young Polish woman, aged twenty-one years, whose epilepsy began soon after puberty and whose mentality was that of feeble-mindedness. Two years ago the mental examination was difficult to make on account of the patient's inability to handle the English language. She spoke Polish. Her answers were prompt, however. She Bineted to the mental age of 6.6 years. The patient stated persistently that she had her first epileptic attacks at seventeen, and that at first they occurred irregularly twice a week. In 1916 she had 84 attacks, which was considerably less than the year before. For the present year the attacks show even fewer than 1916. The present test, however, shows that she is of the mental age of 5.8 years, a loss of a year in mental grading. Her demeanor was quiet and friendly. There was quite marked slowness in word-association, such as for girl, rain and island; the responses were all over thirty seconds. Her memory was fair; she still had a nervous manner in talking. She still has a poor knowledge of English. The clinical facts, including the diminution of epileptic attacks, are rather at

variance with the psychological testing. The latter showed that there was an increasing deterioration upon a primary inferior mental endowment. The deterioration was shown in an increased emotional poverty of ideas, perseveration and an increased slowing of the process of thought.

CASE V.—The final case, Rosa C., is that of a young married woman, aged twenty-nine years, whose epilepsy began at sixteen years of age. She had been married and was pregnant eight months at the time. It was a poor marriage and against the parents' advice. The husband drank to excess and the patient greatly feared bearing children, and was much worried before the first attack. Two years ago she Bineted 9.8 years. On the form board she gave only fair results. The picture-completion test was disproportionately good. Coöperation, interest and attention were good. She was quick to react. Her manner was open and friendly and cheery. Her attacks, which occurred about three a week two years ago, are now a little less frequent, being but one or two a week. Her present mental testing shows she is 9.6, which is only a little less than that shown two years ago. Her reaction time was much better than the others tested in this series; her longest reactions in simple words were eighteen and twenty-two seconds. Her demeanor was quiet and friendly and her attention was good throughout. She says simple, silly things, gives the nurses no trouble and helps at the scrubbing, but her work is not dependable. She is rarely excited.

Here we have a less conclusive case for the relative value of clinical and psychological testings. There is an improvement in regard to seizures and a somewhat better adaptation to her life and work, although the latter is rather poorer than formerly. Psychologically the testing showed a slight retrogression, hardly conclusive enough, however, to possess a deteriorating significance.

In conclusion we may say that the data here presented, while too few for any general statement, are of sufficient clinical importance to show that we must not depend upon a diminution of the epileptic attacks solely in an epileptic to warrant giving a better prognosis, but that the clinical facts of improvement in character and conduct, and kind of work, are to be included. We must also incorporate a more precise mental testing by simple psychological means. Unless all three groups of facts are relatively in accord one ought not to make a positive prognosis of improvement or deterioration in any given case. In time we hope to simplify the psychological testing so that it may be easily performed in ordinary office practice. It is, however, already evident that the single word-association test will enable the physician to judge of the degree of perseveration and the length of reaction time, which are the main criteria for determining the presence and amount of mental deterioration.

## GUMMOUS SYPHILIS OF THE THYROID GLAND.

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Lancereaux<sup>1</sup> in his text *Traite historique et pratique de la syphilis*, published in 1868, wrote "We do not know of any ease which gives evidence of a gummous deposit in the substance of the thyroid gland." Although that statement could not be made truthfully at the present time, the number of reported eases of late syphilis of the thyroid gland are surprisingly few, and in the light of our present knowledge we must regard it as an unusual manifestation of the disease.

The following case was seen at the University Hospital during March, 1916:

Mr. W. P., entered the University Hospital because of the presence of a swelling in the neck and of discharging sinuses over the upper part of the chest. The family history was negative. The patient is married, his wife living and well, and he has three healthy children. One child, the first born, died two days following birth, prolonged labor being the cause assigned. The patient's past history was uneventful. He denied gonorrheal infection, and no history of a chancre could be obtained. He denied premarital or extramarital exposure. Seven years ago he suffered from loss of appetite and "general weakness," and about this time he had a number of reddish sores, covered with whitish membranes, in the mouth. These sores persisted for eight months, new ones appearing as the older ones disappeared. There were no other symptoms suggestive of secondary syphilis at this time, although he states that his eyes tired easily, and while they were not inflamed or painful the vision in the left eye became less acute and has remained so ever since.

The appearance of the thyroid tumor was preceded by various lesions. About three years ago he noticed a swelling the size of the palm of the hand over the upper part of the sternum. This was painless and did not involve the overlying skin, which was of normal color. Fifteen months ago he was struck forcibly at the site of the swelling. A week later the skin over the tumor had become reddened and the color gradually deepened until at the end of the second week it was a purplish blue. Four days later the skin began to ulcerate and he visited a physician. The latter curetted away a large mass of necrotic tissue, and although this procedure was carried out without an anesthetic it was entirely painless. The

<sup>1</sup> *Traite hist. et pratique de la syphilis*, 1868, i, 377.

ulcer refused to heal, however, but increased in size. Two months later his doctor made a vertical incision, about three inches long, through the center of the ulcer, resected the surrounding skin and curetted the sternum and the proximal portion of each clavicle. The ulcer then began to heal and in about three months was replaced by a firm scar. Nine months ago a new swelling appeared in the upper portion of the scar. This was also painless and the overlying skin was uninvolved. Two months later this growth was incised and healing followed, although it was two months before recovery was complete. Meanwhile the patient had been subjected to another trauma, this time at the costochondral junction at the lower third of the sternum. Almost at once a slightly tender swelling appeared. This reached the size of a walnut and persisted until the patient entered the hospital. About the time that the tumor, which appeared in the scar, was excised a small swelling appeared near the left sternoclavicular junction. Three months later the skin over this tumor began to ulcerate and an opening was formed through which a profuse purulent discharge came, and the latter continued until he entered the hospital. A month before this ulcer appeared, still another small swelling appeared over the sternum, just above the right sternoclavicular articulation. This broke down about two months later, resulting in the formation of a sinus with a purulent discharge. This discharge likewise continued until the patient entered the hospital. The patient was unable to remember the exact time of the appearance of the thyroid swelling, but he stated that it began about one year ago. The thyroid tumor was very hard from its beginning, and continued to increase in size rather rapidly up to the time we first saw him. The cervical glands on the left side had been slightly enlarged for some time before the thyroid tumor appeared, but increased in size rapidly along with the latter, and the skin over them became reddened and somewhat fixed to the underlying tissues.

*Examination.* The patient was a tall, fairly well-nourished man. Scalp and skin of the face were clean. The pupils were equal, but reacted sluggishly to light. At the upper end of the sternum was a spoon-shaped ulceration, located at the center of a patch of dense scar tissue nearly as large as the hand. Just above this two small, sharply punched-out ulcers were seen, one above each sternoclavicular articulation. There was a considerable purulent discharge from these ulcers. A probe passed into the ulcer at the left could be introduced easily for a distance upward of about two inches, and it was then found that its end lay deep in the substance of the enlarged left lobe of the thyroid, which could be moved easily with the probe.

The thyroid tumor was confined to the left lobe of the gland and a small portion of the adjacent isthmus. The swelling was about the size of a hen's egg, presented a rather uneven, nodular surface, and was very firm, having a decidedly rubbery consistency. The tumor and ulcers were entirely painless.

The anterior cervical glands, especially along the lower portion of the chain, showed a shotty enlargement, and the skin over them was reddened and somewhat fixed to the underlying tissues.

At the costochondral junction of the sixth rib there was a hickory-nut-sized, painless, hard tumor, fixed to the overlying tissues and skin. Both testes were hard and showed some nodulation at the upper poles. There was also a marked hydrocele.

The mucous membranes were clean. The glands, aside from those already described, were not enlarged. The biceps, triceps and knee-reflexes were normal, but the left Achilles reflex was lost and there was analgesia of the left Achilles tendon. The spleen was easily palpable, a firm edge being felt about one finger-breadth below the costal margin.

Examination of the lungs showed slight impairment at the front and back of the right apex, but no signs of any active pulmonary disease. Roentgenological examination of the lungs showed absolutely no signs of tuberculosis.

In spite of the fact that the patient had experienced no difficulty in breathing or swallowing, he was referred to the department of otolaryngology for examination, and the larynx was found to be entirely normal, the vocal cords approximating perfectly. Fluoroscopic examination following deglutition of barium lactate showed the esophagus to be of normal contour, while a roentgenogram showed the trachea to be of uniform diameter and with normal narrowing at the glottis.

Although the patient vehemently denied that he had ever contracted syphilis, a diagnosis of thyroid syphilis was made. The other conditions considered were tuberculosis and malignancy.

Two days later the Wassermann was reported to be four plus, thus substantiating the clinical diagnosis, and the patient was advised to return to the hospital for antisyphilitic treatment. He again entered the hospital, and at that time was given an injection of 0.3 gm. arsenobenzol (Schamberg), and received potassium iodide in large doses. On the fourth day after the first injection the ulcerative lesions had already begun to heal. The injections of arsenobenzol were continued thereafter weekly in dosages of 0.6 gm. for six weeks. Eight days after the first injection the spoon-shaped ulcer over the sternum had practically healed, the gummatous node at the sixth rib had grown much smaller, and the two suprasternal ulcers were much smaller, although the probe could still be passed easily through the larger one and into the thyroid. The thyroid swelling was also considerably smaller. Within four weeks the suprasternal ulcers were practically healed and the probe could be passed only with difficulty. Two weeks later, when the patient reported for his sixth injection, the ulcerative lesions were completely healed and the thyroid swelling was not larger than a small walnut. The tumor was still very hard. The testicular swellings and the hydrocele were likewise somewhat reduced in size.



It is unfortunate that microscopic sections were not made, but it was not deemed advisable to interfere with the thyroid gland surgically, and no specimen was secured. The diagnosis would seem to be established beyond question, however, without the aid of the microscope. The presence of typical, painless, sharply punched-out ulcers over the sternum, with nodular gummatous lesions elsewhere, the positive Wassermann reaction and the ready response to antisyphilitic treatment of the thyroid tumor together with the other lesions would seem to justify the diagnosis.

Davis in an article published in 1910 enumerates 20 cases of tertiary syphilis of the thyroid in the literature, including his own. It does not seem, however, that all of these cases can be accepted as cases of tertiary thyroid syphilis. For example, the only data obtained concerning Abraham's cases were found in Richardson's<sup>2</sup> text, where the reference not being given the latter says: "Abraham reports 3 cases of women who developed exophthalmic goiter, the first five months after the primary lesion, the second during the height of the secondary infection and the third two years after infection, all of whom were cured by antisyphilitic treatment." These cases are therefore apparently reported as examples of exophthalmic goiter, developing during the course of syphilis and not as thyroid tumors of the gummatous type. Furthermore, in point of time, the first 2 cases may much better be considered as changes occurring in the thyroid during secondary syphilis, a not uncommon finding. The last case, in which exophthalmic goiter appeared two years following infection, must be regarded as a case of exophthalmic goiter of syphilitic origin and not as a gummatous lesion developing in the gland. Such a case was recently reported by Clarke,<sup>3</sup> the exophthalmic goiter in his case being unquestionably of syphilitic origin. All of the remaining cases may apparently be accepted as examples of the condition under consideration, and inasmuch as considerable variation in the thyroid lesions exists in different cases, it seems advisable to review them briefly in their chronological order.

The earliest mention of gummatous lesions of the thyroid is found in an article by Demme.<sup>4</sup> His 3 cases occurred in infants, the victims of hereditary syphilis. He states that syphilis of the thyroid is found in lues hereditaria in the form of gummatous nodes. He saw 2 cases of this type, which, in addition, showed at autopsy definite syphilitic lesions of the liver. A third case showed gummatous nodes in the spleen as well. In all of these cases pustular syphilids of the skin were present. The gummatous tumors of the thyroid were of varying size, grayish or grayish yellow in color and sharply demarcated, like malignant or tuberculous nodules; in one of the cases a single node showed a soft jelly-like consistency.

<sup>2</sup> Diseases of the Thyroid and Parathyroid Glands, 1905, p. 140.

<sup>3</sup> Jour. Am. Med. Assn., 1914, lxiii, 1951.

<sup>4</sup> Krankheiten der Schilddrüsen, Bern, 1878, iii.

In 1883 Wolfer<sup>5</sup> wrote that syphilis of the thyroid existed, but that there had been no accurate investigation of the subject. He stated that Navratil reported a case with a gumma the size of the fist, but that histological confirmation was lacking. Unfortunately, I was unable to secure Navratil's original article.

Barth and Gombault<sup>6</sup> reported the first case of tertiary thyroid syphilis in an adult in whom histological confirmation was presented. The patient was a woman, age not given. The lesion was a swelling of the thyroid, but was not described carefully. No respiratory symptoms were occasioned, nor was any pathology of the respiratory system present. No mention of treatment is made.

In 1887 Fraenkel<sup>7</sup> reported an interesting case: The patient, a woman, aged forty-two years, succumbed and came to autopsy. She had had a cough for two years, which was thought to be due to pulmonary tuberculosis but investigation showed it to be due to syphilitic ulceration of the trachea, this being the dominating features of the case. The thyroid involvement concerned the isthmus mainly, a small portion of the right lobe being affected as well. The tumor was a small one, having a consistency different from that of the rest of the gland, grayish yellow in color and not well demarcated from the surrounding tissue. The tumor was firmly adherent to the larynx. Among many other findings indicative of syphilis at autopsy were nodular gummata of the liver and right kidney.

In 1892 Kohler<sup>8</sup> recorded the case of a woman, aged forty-three years, who had had a swelling of the neck during youth, but was otherwise well. In November, 1891, she was troubled with chills, nocturnal headaches, dizziness and fainting. At the same time she noticed swelling of the skin of the face, hands and neck. The case was obviously one of myxedema. In February, 1891, the symptoms were less marked and the diagnosis was not so apparent. At this time it was noticed that there was a swelling at the anterior part of the neck differing from that caused by the edema. It was hard, subcutaneous and showed several nodular prominences. The patient was operated some time later and the tumor, which was found to be located in the thyroid gland, looked like a broken-down gumma when removed, but the cut surface showed a solid tumor of grayish to grayish-yellow color. Antisyphilitic treatment gave splendid results, the swelling disappearing entirely, while an ulcer which had been present over the sternocleidomastoid muscle healed rapidly. The remaining thyroid gland was of normal consistency and thyroid function was restored.

Two years later Pospelow<sup>9</sup> reported the case of a man, aged

<sup>5</sup> Arch. f. klin. Chir., 1883, xxix, 827.

<sup>6</sup> Progrès méd., 1884, xii, 834.

<sup>7</sup> Deutsch. med. Wchnschr., 1887, xiii, 1035.

<sup>8</sup> Berlin. klin. Wchnschr., 1893, xxix, 743.

<sup>9</sup> Monatschr. f. prakt. Dermat., 1894, xix, 125.

forty-five years, who, after many recurrent syphilitic manifestations, developed diabetes insipidus and a tumor of the thyroid, in association with which there were also some symptoms of myxedema. Both the diabetes and thyroid condition responded readily to treatment with mercury and iodide.

The next report was that of Bruce Clarke<sup>10</sup> (1897). His patient, a woman, aged thirty-eight years, showed a hard, cylindrical tumor of the thyroid gland, reaching from the hyoid bone to the top of the sternum. There was a typical punched-out, gummatous ulcer of the skin near the upper margin of this tumor. The patient complained of difficulty in breathing and swallowing. Previous to the appearance of this tumor the patient had had numerous gummatous ulcers of other parts, all of which had disappeared rapidly under treatment with potassium iodide. The thyroid tumor did not respond well to this treatment and tracheotomy was necessary. After the operation the use of potassium iodide was resumed and the tumor rapidly disappeared, although considerable sloughing occurred.

Küttner<sup>11</sup> reports the case of a man, aged twenty-seven years, who had had a goiter since childhood. For several years before he was seen by Küttner he had noticed moderate dyspnea on exercising. Two weeks previous to his appearance at the clinic he had a severe attack of dyspnea. At this time his breathing was very stridulous even when he was at rest. The right lobe of the thyroid gland showed a fist-sized swelling. This was very hard, was not easily movable and seemed cemented in the tissues of the neck. The tumor was partly retrosternal and had pushed the trachea far to the left. Laryngeal examination disclosed a right-sided recurrent paralysis. The left lobe of the gland was also enlarged, but was soft and easily movable. The clinical diagnosis was carcinoma. Operation was attempted, but the tumor was so firmly adherent to the trachea and other structures of the neck that only a small portion was removed for microscopic examination. Since the histological findings suggested syphilis the patient was given large doses of potassium iodide. The tumor disappeared rapidly and the patient soon breathed freely. When seen six months after the operation he was in good health and had been working steadily.

Küttner also reported the case of a woman, aged thirty-nine years, who had had a small goiter since childhood. She contracted syphilis at the age of eighteen years. For the past four months she had noticed an enlargement of the thyroid and had also noticed that the gland was becoming harder. She soon began to complain of dyspnea. Upon examination a fist-sized swelling of the left lobe of the gland extending from the angle of the jaw to the sternum was found. The tumor was fairly movable, easily palpable, very hard and presented

<sup>10</sup> *Lancet*, London, 1897, ii, 389.

<sup>11</sup> *Beitr. f. klin. Chir.*, 1898, xxii, 517.

a nodular surface. It was covered by normal skin. There was a left-sided, recurrent paralysis and a definite stridor developed when the patient exercised. A diagnosis of carcinoma was made and the left lobe of the gland removed. A number of enlarged cervical glands were also excised. Recovery was uneventful and the patient was discharged. The diagnosis of syphilis was then made, with the histological picture as its basis. She returned five months later with a syphilitic ulceration of the soft palate and the lateral palatine arch. The thyroid gland was still in good condition and she had no difficulty with her breathing. The ulcer of the palate disappeared quickly under treatment with potassium iodide. When seen five years later her health was very good.

Wermann<sup>12</sup> recorded, in 1900, the case of a man, aged twenty-four years, who gave a history of a very active syphilitic infection. For five years following his infection he had suffered many syphilitic accidents. The sixth year the patient's neck enlarged rapidly, due to a symmetrical swelling of the thyroid gland. The condition seemed to be a simple goiter, unaccompanied by symptoms. The gland was uniformly enlarged, soft and painless. The swelling did not subside under treatment with potassium iodide, but as soon as mercurials were employed the tumor rapidly decreased in size. Wermann thought that this was unquestionably a syphilitic manifestation, inasmuch as it appeared while the patient was taking potassium iodide, and although it remained uninfluenced by this drug, involuted rapidly under mercurial treatment.

Mendel's<sup>13</sup> 3 cases, all occurring in women, were reported in 1906. The first patient, aged thirty-eight years, had had a swelling in the neck at twelve years of age. Six months before she was seen by Mendel this swelling increased rapidly, reaching the size of a child's head. The tumor, which was hard and nodular, affected the right side of the gland. Dyspnea was so great that a tracheotomy was performed and the gland extirpated, but the patient died two days later as a result of heart failure. Autopsy showed syphilitic involvement of the spleen and liver as well.

The second patient, a woman, aged thirty-eight years, developed a hard, nodular tumor, the size of a hen's egg, in the left thyroid lobe. This tumor was of three months' duration, and following administration of potassium iodide disappeared completely.

The third patient, aged sixty-three years, had had a slight enlargement of the left thyroid lobe for some time, but suddenly a hard tumor developed in the same lobe. This caused dysphagia and dyspnea, and after five months a tracheotomy had to be performed, a diagnosis of inoperable carcinoma having been reached. The esophagus was also involved extensively. Three months later the tumor reached from one angle of the jaw to the other, and the patient

<sup>12</sup> Berlin. Klin. Wchnschr., 1900, xxvii, 122.

<sup>13</sup> Med. Klin., 1906, ii, 833.

suffered attacks of dyspnea and heart weakness. Inasmuch as the slightly swollen glands of the neck did not have the consistency of cancerous glands, and as there was no ulceration or metastasis, anti-syphilitic treatment was begun. The tumor disappeared rapidly, and in six weeks' time, the cannula having been removed, she was discharged as cured. But in six weeks she returned with a hard, painful tumor of the left lobe of the thyroid, which speedily involved all the tissues of the neck, and death ensued in six weeks. Mendel considered this case as one of malignant change following a syphilitic gumma.

D'Arcy Power<sup>14</sup> records the case of a man, aged fifty-three years, who had contracted syphilis thirty years ago and had had various tertiary manifestations since. When seen by Power he had a tumor of the neck which had been present for one month. The growth was an oval-shaped lesion involving the right lobe of the thyroid gland. It was hard, had a smooth surface and rounded margin and was painless. The swelling was about two inches in length and one inch in width, extending obliquely upward and outward from the episternal notch to a point one inch above the clavicle. The growth was not adherent to the surrounding tissues and did not move on swallowing. The outer end was so hard that it was thought to be calcified. The skin overlying the lesion was normal. Complete recovery followed one month's treatment with potassium iodide and ammonium carbonate.

In 1912 Poncet and Leriche<sup>15</sup> saw a woman, aged thirty-eight years, who had had for the past six months a diffuse swelling of the thyroid gland, more marked on the right side. This tumor was so hard that it was almost wooden in consistency and had begun to infiltrate the other tissues of the neck. The growth had compressed the larynx, giving rise to dysphagia, dyspnea and hoarseness. Treatment with potassium iodide and mercury caused the tumor to disappear, but it soon returned, with the symptoms more marked than before. This time the tumor failed to respond to the same treatment, but involuted rapidly when salvarsan was employed.

Two cases of thyroid syphilis were reported by Sebileau.<sup>16</sup> A woman, aged twenty-eight years, came to him for treatment of a swelling of the neck. Examination showed a hard, painless swelling of the thyroid the size of an orange. This so interfered with respiration that a diagnosis of cancer was made and operation was attempted. The tumor could not be removed, however, as it was fused at the trachea, the rings of the latter being completely degenerated. Potassium iodide and mercury produced a speedy recovery.

The next case was a man, age not given, who showed a goiter-like tumor, firmly adherent to the surrounding tissues, and clinically of

<sup>14</sup> *System of Syphilis*, 1908, ii, 168.

<sup>15</sup> *Bull. et mém. Soc. de chir. de Paris*, 1912, xxxviii, 783.

<sup>16</sup> *Ibid.*, 1911, xxvii, 1305.

an appearance typically malignant. Buds of this tumor projected into the lumen of the trachea. Recalling the last case, antisypilitic treatment was instituted and complete recovery followed.

The most recent case reported is that of Lloyd Thompson.<sup>17</sup> A man, aged seventy-two years, giving a history of syphilitic infection, had suffered four years previously with tachycardia and palpitation of the heart, had lost weight and felt weak and had albumin in the urine. When seen by Thompson there was present a tumor of the neck in the region of the right lobe of the thyroid gland. The growth was about 10 cm. long, 4 cm. wide and seemed to be about 2 cm. in thickness. The tumor was movable and painless. There was slight protrusion of the eyes. The Wassermann reaction was four plus. Under treatment with mercury and potassium iodide the tumor rapidly disappeared, and in six weeks' time was barely palpable. The pulse and blood-pressure, both of which had been high, also returned to normal, and albuminuria, which had been fairly marked became so diminished, that only a trace of albumin was present.

In addition to these reported cases there is on exhibition in the Museum of the Royal College of Surgeons a specimen of gummatous syphilis of the thyroid gland. The trachea is somewhat stenosed as a result of the thyroid tumor.

The total number of authentic cases recorded then, including the present case and that of Navratil, is 23. The ages of the patients varied from infancy to seventy-two years, the majority of the cases occurring in middle-aged individuals. Three of the cases, those of Demme, occurred in heredosyphilitics, while a fourth case undoubtedly belongs in this category. Of the remaining 16 either history or previous luetic manifestations stamped the patient as syphilitic in ten instances. In the remaining cases the histological findings, either at operation or autopsy, or the effect of treatment, must be relied upon as evidence that the individual was suffering with syphilis.

In only 18 of the 22 cases was the sex of the patient reported, being omitted in Demme's 3 cases and in 1 adult case. Syphilitic involvement of the thyroid shows a marked preponderance in the female sex, 11 of the 18 occurring in this sex, a proportion of nearly 2 to 1. When we consider that syphilis is much more common in the male this difference is even more striking. The transient changes occurring in the thyroid in secondary syphilis are also seen much more frequently in women, and the question as to why syphilis, like goiter, should attack the thyroid gland so much more frequently in women than in men offers an interesting field for speculation.

Thompson states in his article that Montgomery has suggested that the comparative infrequency of tabes dorsalis and general paresis in women might be due to the greater activity of the thyroid

<sup>17</sup> Am. Jour. Syph., 1916, i.

in this sex on the theory that iodothylin, the principal constituent of the thyroid secretion, exerted specific influence on the *Treponema pallida*, and so modified them as to prevent neural syphilis. This theory is hardly tenable in the light of the present statistics, showing a preponderance of syphilis of the thyroid in the female.

Among those cases in which a history of the early infection could be secured, the shortest time in which the thyroid became involved was two years and the longest was thirty years.

In 3 cases symptoms due to interference with the thyroid functions were occasioned, and in 2 of these the changes were those seen in myxedema, while in the third (Thompson's) symptoms of Basedow's disease were present—exophthalmos, tachycardia and albuminuria.

In a number of cases were present symptoms due to interference with the respiration and deglutition. In 2 cases dyspnea and dysphagia were present; in another these symptoms with hoarseness as well. One patient complained of dyspnea, stridor and cyanosis; another of dyspnea and coughing; a third of dyspnea alone. In another stridor was the only symptom, and in a fifth coughing alone. Lastly, the specimen in the Royal Museum showed a tracheal stenosis, and it is reasonable to suppose that there was some respiratory difficulty as a result of this. In the remaining cases respiratory symptoms were either not present or were not mentioned. Thus we see that in at least 9 of the cases, nearly 50 per cent., there were symptoms due to interference with the respiratory passages.

Clinical examination, operation or autopsy showed in 9 cases also there was actual pathology of the larynx, trachea or esophagus. Tracheal stenosis occurred three times, esophageal stenosis once and tracheal ulceration once. Recurrent paralysis was found twice, and in one of these cases the trachea was also pushed aside by the thyroid tumor. In one instance the trachea was fused with the tumor and in another the larynx was similarly affected.

Comparing the cases mentioned in the last two groups we find that in 1 case dyspnea and dysphagia were present, with no definite pathology mentioned, while in another, that in which the tumor was fused with the larynx, no symptoms of interference with respiration were noted. Thus in a total of 10 cases, practically 50 per cent. of the total number, there was present some interference with the organs of respiration or swallowing, or both.

The cases which came to autopsy all showed syphilitic involvement of other parts. In a total of 6 cases which were examined post-mortem hepatic gummata were present in all, the spleen was involved twice and the kidneys once.

A consideration of the type of lesion of the thyroid gland showed that the usual tumor was a very hard growth, this type occurring seventeen times. In 9 of these 17 cases the tumor showed a nodular, uneven surface, while in 7 the surface was smooth. In the other cases the contour of the tumor was not described.

Of the remaining 5 cases the tumor was in 2 instances soft, while in the other 3 its consistency was not mentioned.

In 5 cases the tumor was apparently an enlargement of the entire gland; in 6 cases the right lobe alone was affected; in 3 the left lobe; and in 1 the isthmus and a small part of the right lobe. In 7 instances the location of the tumors in the gland was not given. The size of the tumors varied from that of a cherry to growths larger than an orange. In most of the cases the lesions reached a considerable size.

The skin over the tumors was involved by ulceration only twice and in only 1 case was pain a symptom.

In one case the gland was involved secondary to perichondrial gumma of the thyroid cartilage; in a second the process began in the larynx and extended to the thyroid. In all remaining cases the gland itself was first involved.

The response of syphilitic lesions of the thyroid to treatment is as prompt as is usual in syphilis of other parts. Most of the cases having been seen before the salvarsan era, mercury and potassium iodide or potassium iodide alone, had been used in the treatment, 11 cases being treated in this way, with complete recovery in all but 1. In this case the tumor disappeared under treatment with potassium iodide and mercury but soon recurred, and was resistant to these drugs. The use of salvarsan, however, produced a rapid disappearance of the tumor. In 1 case death resulted from the thyroid tumor, but the patient was almost moribund when seen, and no treatment had been instituted. Another case died as a result of other conditions, while Demme's cases of inherited syphilis all died, undoubtedly due to their general condition. One of Mendel's cases, after recovering from what was apparently a gumma of the thyroid, died of cancer of this gland. In 2 cases the tumor was extirpated before a correct diagnosis was made, while in 2 others no mention of treatment or its results was made.

A realization of the possibility of tertiary syphilis of the thyroid gland is important because of the close resemblance which the tumor bears to a malignant growth. In 5 of the cases in this series a diagnosis of carcinoma was made, with operation in at least 4 of them. In still another case operation was advised but not attempted, while in a number of other cases the correct diagnosis was only reached following the autopsy or operation.

The duration of the thyroid involvement varied in the different cases from two weeks to three years. In the majority of the cases the tumors grew rapidly until they reached a certain size and then persisted with little or no increase in size.

Histological reports were given in 12 of the reported cases, and while in the majority of them the diagnosis was rendered easy by a characteristic microscopic picture, in others the findings were less definite.

Demme contented himself with the statement that in the 3



infantile cases the changes in the thyroid corresponded to those usually seen in gummata of the liver, so we may assume that here the histological findings were characteristic of syphilis.

In the case of Barth and Gombault the tumor consisted of a caseous center surrounded by a thick wall of connective tissue, the latter showing a large number of embryonic connective-tissue cells and a few giant cells. *There was also a small round-cell infiltration and some obliterating endarteritis.* Fraenkel found only an infiltration of small round cells. As giant cells, plasma cells and obliterative endarteritis were all lacking it would have been impossible to have made a diagnosis of syphilis on the microscopic findings alone. The specimen exhibited in the Museum of the Royal College of Surgeons showed only a fibrous tissue richly studded with nuclei.

In Küttner's first case gross section of the gland showed some remnants of thyroid tissue near the periphery of the gland, but elsewhere the parenchyma of the gland had been replaced by a gray, homogeneous tissue containing nut-sized caseous nodules. Microscopically these nodules were seen to be surrounded by a zone of giant and lymphoid cells. In the second case he states that the findings were very suggestive of syphilis. But little of the stroma of the gland was present and there was a marked round-cell infiltration. Giant cells and necrosis were lacking, but some of the vessels showed a thickening of the intima and a round-cell infiltration of the adventitia. The capillaries showed a thickening and increase in number of the endothelial cells.

In one case of Mendel's in which sections were examined he found connective-tissue strands radiating from the periphery of the gland inward. Remnants of the thyroid tissue were seen at the periphery of the gland. The center was a structureless mass with some endarteritis present. About the caseous center was an intermediate zone of spindle-shaped and giant cells.

Specimens from Clarke's case showed a typical gummatous structure, with complete destruction of thyroid tissue. Poncet and Leriche found an inflammatory granuloma histologically, exhibiting large numbers of giant cells in the midst of cellular elements of embryonal aspect. No endarteritis was present. The granuloma was so acutely inflammatory that in this respect it resembled syphilis less than tuberculosis. Davis, with a large quantity of material obtained at autopsy, was able to give a thorough description of the macroscopic and microscopic changes in his case. The thyroid tissue had been completely replaced in some places by a new growth, these areas as a rule being sharply demarcated from the surrounding tissue. The tissue comprising the new growths was divided into two zones, the outer of which was made up mainly of large spindle-shaped cells in a myxomatous matrix, but included also a few large stellate and epithelioid cells, and several giant cells. The inner zone was composed of necrotic material, with a few large

spindle, stellate and endothelial cells. Davis felt that the histological diagnosis was unquestionably syphilis.

SUMMARY. 1. Gummatous syphilis of the thyroid gland is of rare occurrence.

2. Women are more frequently the subjects than men.

3. The cases so closely resemble carcinoma clinically that a differential diagnosis on these grounds alone is often impossible.

4. The usual change is a hard, nodular or smooth tumor involving either lobe, the isthmus or the whole gland.

5. Symptoms due to thyroid disturbance are unusual, and when they occur are those of myxedema, or apparently rarely those of hyperthyroidism. Symptoms due to interference with respiration are very common, and may be so severe as to cause death.

6. If the patient is seen before death is imminent and anti-syphilitic treatment instituted the prognosis is very good.

I wish to express my appreciation to Prof. Udo J. Wile for the privilege of reporting this case and for his invaluable criticism.

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## THE DIFFERENTIAL DIAGNOSIS OF AFFECTIONS OF THE RIGHT UPPER QUADRANT.\*

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THE differential diagnosis of affections of the right upper quadrant resolves itself into an interpretation of the various forms of "dyspepsia." Dyspepsia, however, is such a protean condition and arises from so many widely divergent causes that its translation into clinical entities is usually difficult. In the phylogenetic development of the gut tube there has come about a radical subdivision in morphology, physiology and function, and the stomach gives forth reflex symptoms from a variety of diseased organs more or less remotely situated.

In an analysis of indigestion we find that approximately 40 per cent. are due to disease within the abdomen but arising from other organs than the stomach: that 40 per cent. are due to causes entirely without the abdomen and that only in 20 per cent. is there organic disease of the stomach.

Vander Hoof<sup>1</sup> analyzed the cause of indigestion in 1000 cases and found that appendicitis was the causal factor in approximately 25 per cent., cholecystitis in 10 per cent., peptic ulcer in 10 per cent., neurosis in 10 per cent., cancer in 5 per cent., visceroptosis,

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intestinal stasis in 10 per cent., while miscellaneous affections of the kidneys, lungs, eyes, etc., constituted approximately 30 per cent. It is a sad diagnostic commentary when 97 out of 1000 tabetics have had a laparotomy for a supposed intra-abdominal lesion,<sup>2</sup> 19 for gastric ulcer, 19 for gall-stones, 18 for appendicitis and 13 for salpingitis, etc.

Cabot<sup>3,4</sup> found from a study of 1000 autopsies at the Massachusetts General Hospital and a comparison with the clinical findings that in gastric cancer a correct diagnosis was made in 72 per cent. In peptic ulcer, including both gastric and duodenal, a correct diagnosis was arrived at in only 26 per cent.

The very marked advance in the technical efficiency of roentgen diagnosis in the last few years shows how rapid has been our diagnostic progress with 67 per cent. correct diagnosis in duodenal ulcer and 80 per cent. correct diagnosis in gastric ulcer,<sup>5</sup> while 95 per cent. of gastric carcinoma are diagnosed by this means.<sup>6</sup>

For all ordinary purposes of diagnosis we rely upon the history which still remains the keystone in the diagnostic arch of affections of the right upper quadrant. Clinically our problem is to differentiate gastroduodenal ulceration, gastric carcinoma, disease of the biliary apparatus, including pancreatitis, appendicitis and to a lesser extent lesions of the kidney and colon.

If we conceive the stomach as exercising properly two main functions, that of motion and secretion, we would reasonably expect that any ulcerative condition in the beginning before active infiltrative changes had occurred would manifest itself by aberrations either in the motor or secretory functions of the stomach. Is there anything distinct in the evolution of gall-bladder disease that demarks it from the evolution of peptic ulcer? Is there anything in the history of chronic appendicitis wherein it differs in sufficient degree to enable us to differentiate reflex gastric distress of appendicular origin from dyspepsia of gastroduodenal ulcer? We believe that the single factor of greatest importance in differential diagnosis is a carefully taken history. The history should be a citation of the facts of the disease from its beginning and in the order of their occurrence, and if properly taken should provide a means of making a clinical diagnosis. By clinical diagnosis we mean that the nature of the pathological process is determined with relative anatomical localization. It is obvious that one of the most prominent factors in the diagnosis of affections of the right upper quadrant is the correct interpretation of the discomfort and pain for which a patient usually consults a doctor. There are certain fundamental characteristics of abdominal pain—its onset, localization, point of election, maximum point of tenderness and the various paths of radiation and reflexion which are of great value in diagnosis, for within their group most of the affections that we must differentiate run true to type. First, let us take up the consideration of affec-

tions of the biliary tract. We prefer to use this generic designation rather than gall-stones, for gall-stones are an incident dependent upon the virulence of the infection. The gall-bladder, the liver, the pancreas and the stomach are embryologically, anatomically, physiologically and pathologically closely related, and should be considered as one physiological system.<sup>7</sup> Infection is the pathological activator of disease of the biliary apparatus, and while it is true that a gall-bladder may be sterile and yet contain stones, infection must have been present at the time the calculi were originally formed. In disease of the gall-bladder only approximately 75 per cent. are associated with stone, the other 25 per cent. represent varying degrees of infection not associated with the formation of calculi. Irrespective of the presence of calculi in disease of the gall-bladder the histories of a large number of cases will be found to present a composite picture in which four well-defined pathological stages are evidenced and which clinically may be translated into four sequential clinical pictures: (1) When the disease is confined to the gall-bladder; (2) when there are attacks of biliary colic; (3) when calculous obstruction to the common duct intervenes with jaundice; (4) when as a result of infection or trauma to the common duct there is an associated or coincident disease of the pancreas.

The early symptoms of gall-bladder disease are vague atypical symptoms of a qualitative dyspepsia. This dyspepsia conforms to no rule, exhibits no periodicity in its onset, and is characterized by variations in the degree of gas production, eructations, sense of fulness and weight or oppression with occasionally tenderness along the right costal margin. There is a characteristic chilly or goose-skin sensation after dinner and occasionally a slight catch in the breath, particularly on the right side, suggesting a pleurisy. This gastric irritability is made worse by greases, fried foods, apples, cheese and gas-producing carbohydrates in general. Occasionally there is an entire cessation of this indigestion, with prolonged periods of comparative gastric relief. After a variable period of time there is introduced into this picture an acute attack of pain, colicky in type, with marked predilection for nocturnal occurrence, and lasting four to six hours, and usually so severe as to require a hypodermic of morphin. This colic comes on without premonition or warning, although there is occasionally a suggestion of an aura in an unusual state of well-being.<sup>8</sup> Its marked and distinct characteristic is that it is of maximum intensity, occurs spontaneously, like lightning, has a short duration, disappears spontaneously, leaving a residual soreness along the right costal margin. The third clinical picture is due to calculous obstruction of the common duct and introduces for the first time the presence of jaundice. There may be a preceding history of gastric distress, interrupted by periods of colic and during one of these attacks of

pain there is a sudden onset of jaundice which reaches a maximum intensity in twenty-four to forty-eight hours, and is associated with a febrile reaction usually so distinct as to suggest a malarial paroxysm with its chill, fever and sweat. This febrile reaction is so short as to give a characteristic intermittent or remittent fever variously described as "steeple-chart" temperature,<sup>9</sup> or the angle of cholangitic infection.<sup>10</sup> When we have a colic associated with jaundice and marked by fever, leukocytosis, etc., and occurring in that order we are warranted in making the diagnosis of calculous disease of the common bile duct.

It must not be forgotten that a calculus which is capable of passing through the cystic duct may pass throughout the common duct into the duodenum without producing any further trouble. There is, however, a great tendency for a stone in the common duct to become lodged at the ampulla of Vater and by accretions of pigment to increase quite rapidly in size. Whether from the presence of stone or the infection or both<sup>11</sup> it was early observed that there was a very marked association between affections of the biliary tract and pancreatitis.<sup>12</sup>

It is interesting to recall that in reporting the statistics of the Mayo Clinic<sup>13</sup> it was found that in 2611 operations on the gall-bladder the pancreas was involved in 7.6 per cent. In 325 operations on the common duct the pancreas was involved in 22 per cent. and in 168 operations for disease of the pancreas 81 per cent. were accompanied by or due to gall-stones. A number of men, Archibald,<sup>14</sup> particularly, have gone so far as to claim chronic pancreatitis is a common abdominal complaint and capable of diagnosis. "Given a case with acute abdominal pain referred chiefly to the upper half of the abdomen, if upon examination one finds the greatest tenderness located in the epigastrium about midway between the umbilicus and the ensiform cartilage, extending perhaps 1 inch or 1½ inches to the right, and in particular a similar distance to the left also, while absent over the gall-bladder region, if further in the history there are absent symptoms of gastric or duodenal ulcer, and there is no evidence of intestinal obstruction, then this case is in all probability one of pancreatitis."<sup>14</sup>

The clinical differentiation of acute pancreatitis is sometimes difficult and the description of Fitz<sup>15</sup> is even today the best epitome upon its diagnosis. "Acute pancreatitis begins with intense pain, especially in the upper abdomen, soon followed by vomiting, that is likely to be more or less obstinate, and not infrequently slight epigastric swelling and tenderness, accompanied with obstinate constipation. A normal or subnormal temperature may be present and symptoms of collapse precede by a few hours death, which is most likely to occur between the second and fourth day."

The history of pancreatic or biliary carcinoma is distinct. The genesis of tumors requires time and the history of the onset of

jaundice is succinct and characteristic. By slow growth a neoplasm produces from day to day only minimal changes, whereas vascular or inflammatory processes produce extensive changes within a short time. Neoplasms of the biliary apparatus, the pancreas or the contiguous portion of the duodenum early invade or compress the termination of the bile and pancreatic ducts. Jaundice develops imperceptibly and without pain, so that from day to day it seems hardly to advance in intensity, but without pause or hesitation, without intermitting or remitting, it progressively deepens in intensity from mild to severe, from lemon to black, until it becomes the typical icterus melas. Its evolution is not associated with colic and in its earlier stages is usually devoid of pain. It is not associated with chills, fever or sweats nor leukocytosis. With such a history, malignancy is the probable diagnosis, and when this history is associated with a palpable or distended gall-bladder the diagnosis is almost positive. One of the few diagnostic laws that has stood the acid test is Courvoisier's law. Courvoisier enunciated his law: "In cases of chronic jaundice, due to blocking of the common duct, a contraction of the gall-bladder signifies that the obstruction is due to stone: A dilatation of the gall-bladder, that the obstruction is due to causes other than stone."<sup>16</sup>

In reporting the cases of the Massachusetts General Hospital, Cabot<sup>17</sup> found that "in 86 cases of obstruction of the common duct 57 were due to calculous obstruction and in 47 the gall-bladder was atrophied, in 8 it was normal and in 2 enlarged. In 29 cases the obstruction was due to causes other than stone. In 27 the gall-bladder was diseased and in 1 the gall-bladder was empty and in 1 contracted around the calculi; 4 cases only of this series were exceptions to Courvoisier's law. With the exception of these 4 cases which constituted only 5 per cent. of the total number examined every record of the Massachusetts General Hospital series in which definite statements are to be found concerning the points at issue goes to confirm Courvoisier's law."

Peptic ulcer is a distinct organic ulceration of the gastroduodenal portion of the gut tube, and within its type the symptoms are constant and, as a rule, characteristic. Variations in symptomatology depend to a considerable extent upon the localization, since 70 per cent. of all peptic ulcers are located so as to interfere with the emptying power of the stomach. In the diagnosis the history is all important. Palpation, percussion and auscultation give evidence of very limited value; chemical examination of gastric contents give some confirmatory value only. The presence of gastric blood will be absent in over 75 per cent. of cases while roentgen-ray examination is positive in 67 to 80 per cent. of cases of duodenal and gastric ulcer respectively. With clinical methods alone we are able to make a correct diagnosis in 80 per cent. of cases. Three

facts stand out in the history of all regular cases of peptic ulcer: (1) Pain; (2) time relation of pain to food ingestion; (3) periodicity of attacks.<sup>18</sup>

In all true ulcers in their symptom-producing stage a given set of symptoms are present or are introduced by certain articles of food or have a certain time interval in relation to the ingestion of food. These symptoms are constant and the interval or period is definite. If beefsteak produces pain upon ingestion then beefsteak during the symptom-producing stage always produces pain quite distinct and characteristic from the neuroses which intermit in their relationship from day to day. In ulcer if the pain is produced one hour after the ingestion of meat that interval is usually constant for the type of ulcer. Now, biologically in the beginning an ulcer manifests itself by irritations of the functions of the stomach and there is the interference or an irritation in the secretory motor functions, and there is the clinical condition of hyperchlorhydria from increased secretion or qualitative changes in acidity, and in the beginning there is usually hypertonus, hyperperistalsis and hypermotility.

The ingestion of food under normal circumstances is accompanied by a reflex process which is not perceived—a subconscious reflex—and when pain arises from the ingestion of food it points to an irritable process of the cord through which these reflexes pass as a result of oft-repeated painful stimuli. The epigastric region is essentially the place to which sensory symptoms are referred and the upper part of the left rectus muscle usually contracts first in response to an irritation from the stomach.<sup>27</sup>

A long history of gastric trouble associated with pain in the lower part of the epigastrium would suggest pyloric stenosis. We may therefore say that the patient with a gastro-duodenal ulcer presents in the main a history characterized by (1) pain, bearing some relation to the ingestion of food and the quality of food; (2) a chronicity; (3) the periodicity or the repetition of symptoms day after day during the symptom-producing period of the ulcer. As a corollary to these three are certain variant characters for certain types of ulcer; the nocturnal pain of duodenal ulcer and its rather specific type of hunger pain. Pain in ulcer follows the ingestion of food after a definite interval which is marked by the order and precision of its occurrence and its persistent occurrence throughout the whole history of the case.<sup>21</sup>

The complex of chronicity and the periodicity of attacks with pain or distress, repeated uniformly day by day during the attack and bearing a fairly definite relation to food intake and control is of primary clinical importance to the diagnosis of 80 per cent. of cases of uncomplicated peptic ulcer. In the remaining 20 per cent. this complex may be irregular, atypical or almost entirely absent, or the symptoms may be mixed, owing to coincidence of

disease of contiguous organs which occurs in about 20 per cent. of all cases of ulcer.<sup>19</sup> In the irregular or atypical 20 per cent. the roentgen-ray examination with a bariumized carbohydrate meal is of great value: (1) By deformities of luminal contour; (2) by the triad of hypers—hypertonus, hyperperistalsis and hypermotility,<sup>20</sup> and of lessened value the determination of aberrations in gastric chemistry.

If an ulcer is situated on the lesser curvature near the cardiac end the symptoms are different than when located at the pylorus or in the duodenum. The symptoms of ulcer near the cardiac end will be those of pain, shortly after eating, with periodicity in its production, with the vomiting of partly digested food, with blood in the vomitus, with a progressive emaciation because the patient does not retain his food. With ulcers involving the pylorus there is soon introduced relative pyloric stenosis from spasm and secondary absolute pyloric stenosis from infiltration and spasm and the symptom of pain after the ingestion of food, when this interval gives place to the vomiting of large quantities of fermented material with food remnants. In the pyloric type of ulcer there is, as a rule, a loss of weight and secondarily a cachexia from absorption of fermented and putrefying gastric content. Now, quite distinct from these two types is that of the duodenal ulcer where the patient is, as a rule, well nourished and when he has food in his stomach is without distress.

Turning to duodenal ulcer, specifically we are in full accord with Moynihan that "persistent recurrent hyperchlorhydria is duodenal ulcer."<sup>21</sup> In gall-bladder disease, pain and discomfort usually come on with eating, while in duodenal ulcer the pain is relieved by eating. In duodenal ulcer the food that gives pain in pyloric ulcer gives relief in duodenal ulcer. The patient with duodenal ulcer, usually a man, is ordinarily a well-nourished individual, with marked appetency for food and who informs you that if he could eat all of the time he never would have a bit of pain. Consider his daily history: He starts out in the morning, eats a good breakfast and about 11 o'clock gets a pain, a pain that is usually described as gnawing, persistent and rather severe, but one that is tolerated. He seldom requires anodynes. He eats a sandwich or drinks a glass of milk and the pain disappears. The pain usually comes on when his stomach is empty and at about the time that he is naturally hungry. For this reason it becomes known as hunger pain. At about 4 o'clock the pain recurs and he takes another light lunch with rapid cessation of pain. Returning home he eats a well-proportioned supper, and before going to bed has a few crackers and a glass of milk. Sometimes about 12 o'clock he is awakened by epigastric pain of the previous type, but rather more severe. Repeated experience with the night pain has made it necessary to have some crackers or a piece of chocolate at his bedside. Upon



eating something or taking soda the pain disappears. This history is repeated day after day with unvarying precision and consistency. Its story is typical and the diagnosis might be made as Moynihan expresses it "by correspondence."

The value of test meals is of confirmatory value only. In order of importance are: (1) food remnants, (2) blood, (3) acidity of test meal.<sup>26</sup>

In considering cancer of the stomach one may say that it makes its presence known only when ulceration occurs or when there is an interference with motor function of the stomach. The history is of most value in suggesting or arousing the suspicion of malignancy. There is, however, no isolated or significant sign or symptom upon which the diagnosis of early cancer can be predicated. The diagnosis of early cancer depends upon the mechanical interference produced, and it is an accident if the location of the growth is such as to introduce early the element of stenosis. If there is any symptom which stands out as between ulcer and cancer it is the known presence of periodicity of symptoms in ulcer and its absence in cancer. Periodicity is present in about 85 per cent. of ulcers and is absent in 99 per cent. of cases when that ulcer becomes malignant.<sup>22</sup>

Cancer of the stomach occurs in three forms: (1) The man who is perfectly well, who has an athletic stomach and who has never had any previous gastric distress. There comes into his history an abrupt sudden development of gastric signs. His symptoms suggest an acute ulcer of the stomach, with hemorrhage, but at the end of three or four weeks the man has lost physically beyond what would be expected of a simple ulcer. His anemia has become more pronounced, with a distaste or aversion for food, and finally from the anemia, emaciation and beginning cachexia the diagnosis of rapidly growing carcinoma is made. This type constitutes about 30 per cent. of all cancer cases and has an average duration of eight to ten months. The second class, and by far the largest proportion of about 60 per cent., is represented by the patient who has a perfectly clear history of chronic gastric ulcer extending over a period of years. A form of gastric distress characterized by periodic discomfort or pain usually bearing a distinct relationship to food ingestion with some vomiting. His previous gastric history covers a period of eight to ten years, with intermittent attacks of typical ulcer history. Finally, there comes an attack from which he does not respond to the medical treatment that heretofore has proved beneficial. The pain becomes constant, marked distaste for food intervenes with particular aversion to meat; blood is constantly present in the stool and vomitus and he has an average duration of cancer symptoms approximating six months. The third class, of about 10 per cent., is represented by the patient who has a typical history of gastric trouble from which

he nearly but never quite recovers, and after a variable period progressively, but very slowly, becomes worse, with a distinct distaste for food and without any interruption progresses to a well-defined cachectic condition of malignancy.

No paper on affections of the right upper quadrant would be complete without considering chronic appendicitis. The commonest site of a "gastric ulcer" is the right ileac fossa.<sup>21</sup> In my personal experience at least 18 per cent. of cases coming to laparotomy have two lesions, either one of which offers an operative indication.

"Appendix dyspepsia" is a varied and indistinct clinical picture. It is usually more difficult to diagnose than either the conditions of ulcer or disease of the gall-bladder. If one can eliminate either of the two conditions named above it would be possible to arrive at a diagnosis of appendicular dyspepsia by elimination. In the ordinary case there is usually an absence of a history of an acute attack. Epigastric distress is a constant annoyance or sense of ache and usually with no distinct relationship to food. The pain or distress is apt to be aggravated by activity and motion and is occasionally relieved by an enema or a cathartic. It is infrequent for appendicular dyspepsia to be associated with a history of acute attacks, although occasionally local appendiceal pain may be elicited.

The chronically diseased appendix induces reflex gastric disturbances and usually contains fecaliths. The mechanism of disease is probably in a large majority of cases a pylorospasm with pain, vomiting, increased secretion, increased acidity, gaseous and sour eructations. It is noteworthy that the pain and distress is usually more prolonged than similar occurrences in disease of the gall-bladder. The distress is usually associated low down in the epigastrium or about the navel and lacks the distinct characters of localization as in biliary disease.

The outstanding features in the genesis of appendicular dyspepsia are its irregularity, variability and almost entire lack of periodicity. Food that at one period is associated with gastric irritability is upon another occasion eaten with zest and no distress. The attacks are distinctly less regular in their symptomatology than in ulcer.

It is interesting to note that McCarty<sup>23</sup> reported 59 cases when both the gall-bladder and appendix were removed and that 69 per cent. of the appendices showed distinct pathological changes. The ordinary postmortem incident of disease of the appendix is approximately 17 per cent.<sup>25</sup> Furthermore, in operations for cholecystitis 52 per cent. were associated with disease of the appendix, and in cholelithiasis 44 per cent. had distinct pathological changes in the appendix.

Paterson<sup>23</sup> found appendicular disease in association with gastric ulcer in 54 per cent. of cases and with duodenal ulcer in 66 per cent. of cases. Hutchinson<sup>24</sup> records 24 cases of fatal hemorrhage from

the stomach after operations of various kinds upon the abdominal viscera. Of these 24, 21 were cases of appendicitis with septic complications. I have records of 4 cases of pronounced gastric hemorrhage which on very extensive abdominal exploration revealed no morbid process except in the appendix, and following an appendectomy there was a cessation of gastric distress and gastric hemorrhage.

Gastric hemorrhage has been experimentally produced by Rogers by injecting chemical irritants into the cecum and ascending colon, while irritation of the colon, *per se*, has been shown to bring about a gastric stasis and the delayed passage of food material through the small intestine.<sup>29</sup>

Barclay<sup>30</sup> quite recently has drawn attention to the spasmodic closure of the pylorus following reflex stimulation from the terminal ileum, when there is a too rapid overloading of the small intestine with chyme. Biologically the ileocecal valve represents a great point of chemical and bacterial partition, for at the cecum we have a change in chemical reaction; maximum bacterial flora, maximum fluidity, anastalsis, predominant lymphoid tissue and a point of natural or normal stasis.<sup>31</sup> These observations would seem to offer proof of a very extensive system of intra-alimentary reflexes acting upon the pyloric mechanism, and it would serve to explain the incidence of appendicular dyspepsia.

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## ROENTGEN RAYS AS AN AID IN THE DIAGNOSIS OF ULCUS VENTRICULI.

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WHEN Cannon visualized the stomach in the animal by feeding it on food mixed with bismuth subnitrate, and Rieder introduced the bismuth meal for the same purpose in the human being, it was hoped that ulcer and cancer of the stomach would be absolutely accessible to diagnosis. While such hope was realized to a fair extent it cannot be too strongly emphasized that in the great majority of cases, especially of ulcer of the stomach, roentgen rays alone without the other clinical methods may quite often be misleading.

Roentgen-ray diagnosis of the diseases of the gastro-intestinal tract in general, and of ulcer of the stomach in particular, owes its development primarily to the Continental workers, notably among whom are to be mentioned Rieder, Holzkecht, Faulhaber, Kreuzfuchs, von Bergmann, Levy-Dorn, Barelay, and Hertz. Not long afterward the Americans began their very painstaking work, and here rank the names of Case, Carman, Pfahler, Jordan, Skinner,

Cole, George, Hirsch, Holden and others. Comparing the aims and accomplishments of European workers with those of our country, one notices throughout that while in Europe most roentgenologists in studying the diseases of the gastro-intestinal tract made every effort to interpret their findings according to the disturbed function caused by existing pathological lesion, in this country more importance was originally attached to structural changes in the roentgen-ray interpretations.

Among the American authors who independently utilized the functional methods of roentgen-ray diagnosis in the study of gastro-intestinal diseases are Case, Carman, Mills, Skinner and Hirsch.

Accordingly, two methods are employed: the indirect method, by which we determine a lesion in the gastro-intestinal tract, based on disturbed function, and the direct method, which bases the diagnosis of a lesion on existing structural changes. Both have their respective usefulness.

From the clinical stand-point, however, there is no doubt that the roentgen studies based on disturbed function (indirect method) are outweighing in importance the direct method. It is an established fact that the patient's complaints are in proportion to the disturbed function of a particular organ. Based on such complaints, plus a thorough physical examination, one establishes a proper diagnosis. The clinician who finds himself so frequently confronted with difficulties, especially when dealing with diseases of the abdominal viscera, at once asks, Will roentgen-ray examination give us information of additional value to make a definite diagnosis when the symptom-complex and the rest of the physical and laboratory examinations have left us in doubt? This, as will be shown, has been realized to a considerable degree.

In the roentgen-ray diagnosis of ulcer of the stomach we seek to determine whether we are dealing with a simple or a complicated lesion. Approaching the roentgen-ray diagnosis of simple ulcer of the stomach from the stand-point of disturbed function (indirect method), we must have a clear understanding of the normal function of the stomach as seen roentgenologically, and hence a brief consideration of the roentgenological physiology is essential.

Roentgen-ray examination enables us to study with exactness the following physiological phenomena:

1. Position and form of the stomach.
2. Tonus and peristalsis.
3. Gastric secretion.
4. Mode of filling and motility.
5. Mobility.

1. POSITION AND FORM OF THE STOMACH. In the great majority of people the stomach lies to the left of the median line, with the exception of the pars pylorica, part of which lies to the right of the median line. The greater curvature in the standing position is

usually either on the line with or 1 or 2 cm. below the crest of the ileum. In a lesser number of cases the stomach lies high in the abdominal cavity, with the pars pylorica entirely to the right of the median line, even part of the corpus to the right. The first more frequent position gives us the form described by Rieder (Fig. 1) as the pipe-shaped stomach, called by Groedel the siphon stomach; the second the less frequent (Fig. 2) is termed by Holzknecht the bull-horn stomach.



FIG. 1.—Pipe-shaped stomach.



FIG. 2.—Bull-horn stomach.

The form and position of the stomach, as shown in the accompanying figures, not being uniformly found in normal individuals, has given rise to considerable discussion by both clinicians and roentgenologists. Such discussions seem justified because the roentgen-ray stomach does not correspond in position and form to that described by the anatomists. This has led no less an authority than Stiller to state that a stomach when containing food with a contrast substance does not exemplify a normal stomach. Roentgenologists again have widely differed in their opinions as to what form is to be considered normal from the roentgen-ray stand-point. Groedel, for example, claims that the roentgen-ray stomach, with the individual standing, cannot be compared with the stomach described by the anatomists, because the latter have always seen the stomach in the cadaver with the corpse in the horizontal position. From such assertions it is evident that the difference in shape and form of the stomach, according to Groedel, is chiefly dependent on the position of the individual and the passive filling of the organ. While this is true to some extent it will be shown below that such an exclusive view leads to erroneous conclusions.

A much more enlightened contribution as to what constitutes a normal form and shape of the stomach and the factors that enter into their formation has been furnished by the laborious work of Forssel. Forssel's work and conclusions we intend to analyze in detail. It seems advisable, however, to name first and demonstrate

by figures the most important roentgenological division of the stomach.

The well-known anatomical division into fundus, corpus and pylorus had to be modified when the stomach was visualized roentgenologically. In view of the fact, however, that different roentgen-

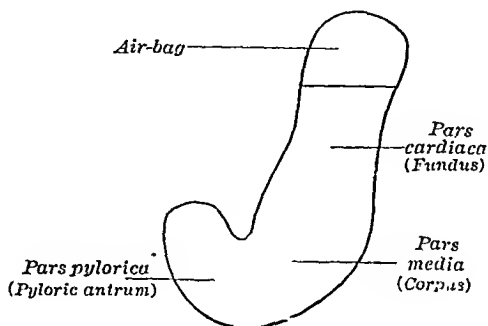


FIG. 3

ologists describe different forms and shapes of the stomach, even in a normal state, a uniform division has not yet been agreed upon. Holz knecht and Huerter divide the stomach into fundus, corpus (pars media) and pars pylorica (Fig. 3). Groedel's division is pars descendens and sac and pars ascendens (antrum and pylorus).

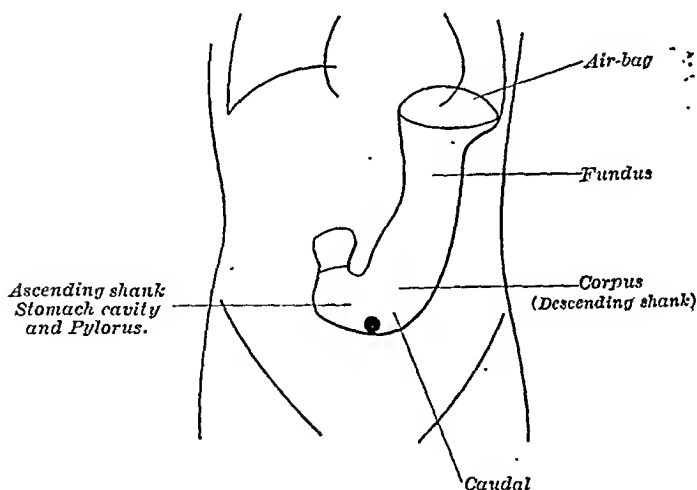


FIG. 4

The uppermost part of the stomach he terms the cranial portion and the lowermost part the caudal portion (Fig. 4). The Holz knecht, Huerter and Groedel division are not exact because the uppermost part, named fundus, would be in reality a fundus only if the individual stood on his head. Holz knecht and Huerter as

well both speak of a pars media and pars pylorica, and ignore the caudal part or connecting link (a very important part to be shown later). Groedel, who speaks of the descending and ascending part, presupposes an ascending portion in every stomach, whereas it is well known that the bull-horn (Holzknecht) type has no ascending part. Furthermore, the connecting link he terms magensack (sac of the stomach), which would imply a passive portion of the stomach when filled with food. In reality that part of the stomach is a very active one.

The objections outlined as to the loose description of roentgen-ray form and position of the stomach, as well as its divisions, are overcome by the painstaking anatomical and physiological studies of Forssell, who showed that the form and the position of the stomach are solely dependent on the work of the musculature of the stomach. E. Schlesinger expressed the view long before Forssell that the form of the stomach depends on its tone, and Holzknecht built up on this basis the classification into ortho-, hyper-, hypo-, and atonic types. Useful as the suggestion of Schlesinger seemed to be, it was soon evident that his work and even the classification of Holzknecht expressed just a visual appreciation of the form without consideration as to the underlying mechanism which constitutes the different forms.

We follow the reasoning of Forssell to show that form and position are dependent on the muscular architecture of the stomach, because an understanding of this architecture is essential to an intelligent interpretation of the fluoroscopic or roentgenographic appearances of the stomach. Forssell showed that the vertical part of the stomach (termed fundus and pars media by Holzknecht and others) has for its support the strong musculature which runs vertically from cardia to antrum, nearer to the lesser than greater curvature, *i. e.*, eccentrically. This musculature forms the well-known groove of Retzius (Magenstrasse of Waldeyer or sulcus gastricus) (Fig. 5), where the food is distributed to the vertical part of the stomach. The musculature forming the groove is therefore the fixed supporting axis around which the musculature of the rest of the vertical portion of the stomach is grouped. The musculature forming the fixed point, situated as it is nearer to the lesser curvature than to the greater, allows distention of the stomach almost exclusively toward the greater curvature, and is therefore responsible for the asymmetry of the vertical portion of the stomach. The lower part of the stomach (pars pylorica), the musculature of which is grouped centrally around its axis, runs transversely in a symmetrical manner. This gives that part of the stomach a tube-like form.

According to Forssell the supporting apparatus of the stomach consists of a vertical and a transverse portion. The vertical apparatus is formed by the median and external layer of the longitudinal bundle as well as a supporting loop of the inner layer;



the transverse portion is formed by the ligamentum transversalis of the transverse portion of the stomach. Besides the supporting apparatus residing in the musculature of the stomach proper, both portions of the stomach have supports from without. The vertical part is intimately connected with the cardia by the phrenicogastric ligaments; the transverse portion is supported at the pylorus by the hepatoduodenal ligament and the musculus suspensorius duodeni. From the anatomical stand-point the division into a vertical and a transverse stomach is very appropriate. Forssell as well as Cunningham, however, go further and divide the stomach according to its function (Fig. 6). The vertical or asymmetrical portion is designated as the corpus digestorius and the transverse portion as the corpus egestorius. The caudal part forms the sinus and the incorrectly formed fundus is changed to the appropriate term fornix.

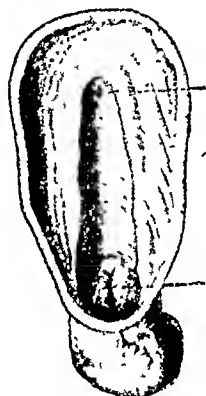


FIG. 5.—Retzius's groove.

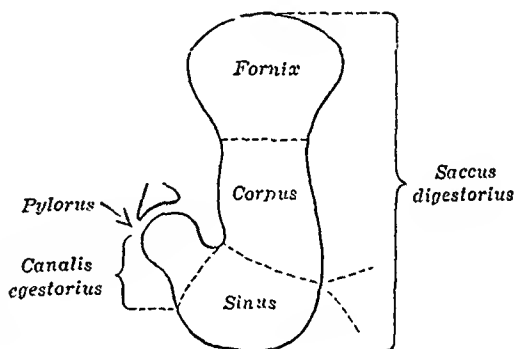


FIG. 6

The two types, bull-horn and siphon, are, according to Forssell, explained in the following manner: The typical changes in the form of the stomach depend on whether the entire corpus digestorius or the sinus alone is in the state of contraction. By contraction of the sinus the stomach approaches the form of a uniformly bent tube or so-called bull-horn type. It is this form which shows the strongest contractions (hypertonic type, Schlesinger). As the supporting apparatus of the vertical portion of the stomach participates in the contraction it brings the entire organ into a higher position, and we therefore find the lower border above the umbilicus. We meet this form in individuals who have a broad thorax with a wide aperture (hypertonic individuals, status apoplecticus), also where there is an increase of intra-abdominal pressure, as in obesity, meteorism, ascites, pregnancy, and when the patient is in the horizontal position. In all such individuals, however, it is not the displacement of the stomach by its surrounding organs but the

stimulus from without which causes excessive contractions in the entire corpus digestorius, bringing about a bull-horn form. When the contractile power of the musculature is lost the bull-horn form cannot be produced by any outside influences. The infant stomach, which is usually of this form, is explained by the stimulating influence of the large liver and distended bowels during the first months of life. The siphon form of Rieder is brought about by the uniform contraction of the entire stomach. Such a stomach has the greater curvature at 1 or 2 cm. below the umbilicus, an out-spoken incisura. The lowest part of the stomach is formed by the sinus. This type is found with the greater part to the left of the median line, only the pylorus reaching the median line, or 1 or 2 cm. to the right.

Which of the two forms shall be considered roentgenologically normal? This can be answered only if we compare the form of the stomach to the status of the individual. Finding as we do the transverse stomach at an early age, up to ten years, as well as between forty-five and sixty, the explanation suggests itself that the stomach will tend to assume the transverse position during those periods, when the individual has a tendency to grow in width rather than in height. In childhood, growth in width consists of the bony and muscular as well as adipose tissue, while after forty-five it is mainly the adipose tissue that determines the increase in width. Whatever it is, the increase of abdominal and intra-abdominal pressure stimulates the stomach musculature to increased contraction, bringing about a transverse position. This is further aided by the high position of the diaphragm through which the external supporting points of the stomach (esophagus and hepatoduodenal ligament) are carried upward. During the age of growth—ten to twenty, with its predominating development in height—and the age of overactivity—twenty to forty-five, with no tendency to add fat—the vertical stomach (Rieder) is the normal. If a transverse stomach situated high in the abdomen is met in individuals of the status apoplecticus it is a normal form for that status. In individuals, on the other hand, who belong to the status asthenicus the long stomach with the greater curvature almost on the symphysis pubis is normal for that type.

It is an established fact that both forms, because of the status, may predispose to organic diseases of the digestive organs, but primarily the organs are not diseased. The transverse stomach predisposes to duodenal ulcer, the very long stomach to a gastric ulcer.

2. TONUS AND PERISTALSIS. A proper understanding of the physiology of peristalsis, its function and its results, is absolutely essential to an appreciation of the changes in the peristalsis of the stomach under pathological conditions of the digestive organs.

As stated above, the stomach is divided, according to Forssell

and Cunningham, into two main compartments. Forssell calls them *pars digestorius* and *pars egestorius*, while Cunningham names them cardiac and pyloric portions. These portions are subdivided, Forssell dividing the *pars digestorius* into a fornix (*pars cardiaca*) terminating at a point corresponding to *incisura cardiaca*; corpus, extending from *incisura cardiaca* to the *incisura angularis*; sinus, from *incisura angularis* to *antrum pylori*. *Pars egestorius* consists of the *antrum pylori*. Cunningham speaks of the *pars cardiaca* as the sac of the stomach. The corpus he terms tube and the rest is the pyloric portion.

Before we proceed, let us take up briefly the term *antrum*. The anatomists and physiologists originally thought that the pylorus was separated from the stomach by a sphincter similar to that of the pyloric sphincter, but later a close study of the pylorus by anatomists failed to demonstrate the existence of a sphincter. They found that on the lesser curvature distal to the *incisura angularis* there is a thickened transverse band of musculature, at which point on the lesser curvature and opposite to which on the greater curvature the contraction wave is deeper. According to the excellent observation of Cannon this deepening never, under normal circumstances, completely separates the pylorus from the rest of the stomach, hence he has rightly named this part "vestibule" instead of the meaningless term *antrum pylori*. Cannon's findings are still further substantiated by the cinematographic studies of Ricder, Koestel, Rosenthal, Cole and others.

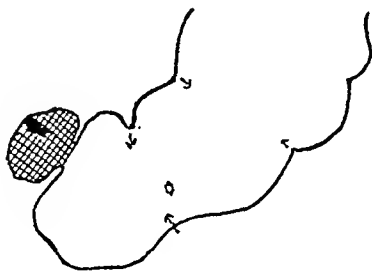


FIG. 7.—Peristalsis.

*Peristalsis as seen Fluoroscopically.* If we observe fluoroscopically the taking of food we note the following as regards normal peristalsis: After the first morsels have reached the vestibule a contraction takes place at the transverse band on the lesser curvature and a similar one at a point opposite on the greater curvature. This peristaltic wave, which we term the initial wave, is a response to the gastric secretions brought about by the act of chewing (appetite juice, Pawlow). Now, as the stomach fills up, we notice a state of repose lasting from four to six minutes, during which no peristalsis is seen in any part of the stomach. After that the regular

peristaltic waves set in. The wave begins at a point on the greater curvature opposite the *ineisura cardiaea* (Fig. 7), running along the greater curvature, forming shallow waves. At a point opposite the *ineisura angularis* the wave deepens. Distal to the *ineisura angularis*, *i. e.*, at the beginning of the vestibule there is a still deeper contraction on the lesser curvature with a correspondingly deep contraction on the greater curvature opposite this point. This contraction lasts longest and achieves a depth almost simulating a division of the stomach into two compartments. In reality, as rightly pointed out by Cannon, a complete separation does not exist under normal conditions. The last two waves named are in fact persisting contractions, the object of which will be discussed later.

The waves do not go any farther than the pyloric ring because of the hiatus between the circular muscular fibers of the stomach and duodenum. Peristaltic waves take place four to six each minute. The part of the stomach above the *ineisura cardiaea* (fornix, cardiac sac) possesses no peristalsis, only a peristole (Stiller) which exercises a firm grasp on its contents. Along the lesser curvature only superficial peristaltic waves are usually observed.

Corresponding to the visualized waves in different parts of the stomach it was experimentally demonstrated by Moritz that there is a difference of the intragastric pressure in the different parts. In the cardiac end it amounts to 6 to 8 cm. water and in the pyloric from 30 to 60 cm.

The importance of the peristaltic waves in relation to gastric digestion is still disputed. The earlier physiologists, Beaumont and Elkin, and some of the more recent workers, like Hofmeister and Sehuetz, assert, on the basis of their experimental work, that the peristalsis in the corpus from *ineisura cardiaea* to the vestibule of the stomach is mainly concerned with churning and mixing of the food, whereas the pylorus merely expels the food.

Cannon was the first to take an active stand against the older teachings that the digestive process goes on mainly in the corpus. He correctly stated that the experiments of the earlier observers produced pathological conditions of the stomach, and hence their conclusions are not physiologically correct. Cannon derived his conclusions from his observations on animals and human beings by means of the roentgen rays, and so his findings correspond nearest to physiology. According to Cannon the fornix (sac) serves as the actual reservoir. From the sac the food is advanced into the tube by the action of the diaphragm, aided by respiratory movements. In the tube (corpus) the food is mixed with the acid secretion and by peristaltic waves is carried acidified to the vestibule (pars pylorica). Part of the food in the tube is squirted back into the reservoir.

In the vestibule, therefore, according to Cannon, active digestion

and churning of the food goes on. According to the same author also, the sac forms the largest part of the stomach in the course of digestion and the tube the thinnest part.

While Cannon has ingeniously attributed to the sac the property of a reservoir in contradistinction to the tube which serves as a motor, we find that he does not account for the part of the stomach between the incisura angularis and the beginning of the vestibule (see Fig. 6), both ends of which are marked by deep peristaltic indentations. It is that part of the stomach that Forssell has termed the sinus.

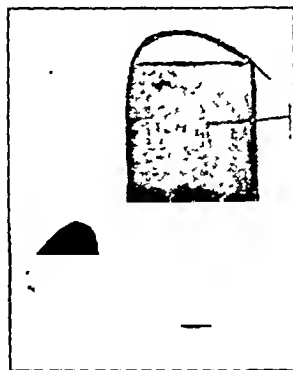
From our roentgenological observations we can state definitely that the greatest peristaltic activity is visible in the sinus. It is also worthy of mention that from the beginning of digestion (initial wave) until the stomach is entirely empty the sinus is seen filled and is the place of greatest peristaltic activity. The reservoir sac forms the largest part of the stomach only in the early stage of digestion, while later in the course of digestion most of the food is seen in the sinus. This would tend to demonstrate that the need for the reservoir diminishes in the course of digestion.

Our conception of the mechanical part of digestion, especially with reference to the mode of peristalsis, is as follows: Like Cannon we believe that the sac is the actual reservoir, and is that part of the stomach in which non-acidified food is stored until it is sent down, little by little, by the active reservoir to the tube to be acidified. From the tube, active peristaltic waves propel the acidified food to the sinus, where it meets pepsin secretion from the peptic glands in the sinus and that imported from the vestibule.

In the sinus the most active peristalsis takes place in order to churn and fully liquefy the food to be ready for the vestibule, whence the food is brought to the sphincter pylori (pyloric canal, Cannon). The reason why the cardiac sac is the largest part in the early stage of digestion is that at first only the fluids and such food as needs less digestion are transferred from the sac. An hour or two later, when secretions and acidity are at their height, the coarser food more difficult of digestion can be taken care of in the sinus; the sac transfers it with greater rapidity and the sinus serves not only as a place of active digestion, but sends it, little by little, as it is made ready, to flow into the vestibule. The activity of peristalsis in the sinus as digestion goes on is, according to our opinion, responsible for the pylorus forming the lowest part during that time of digestion, an observation first made by Cannon and von Bergman. Active contraction in the sinus shortens that part, making the pylorus appear as the lowest part.

Passage of food through the sphincter pylori is brought about by the acid reflex (Cannon) on the pyloric side opening the sphincter. Closure of the pylorus is accomplished by the acid reaching the first portion of the duodenum (Hirsch, Pawlow and Mering).

3. GASTRIC SECRETION. Gastric secretion was first roentgeno-logically described by E. Schlesinger. Normally it manifests itself only as a small intermediary layer between the air-bag and the corpus when the contrast meal is given (Fig. 8). The intermediary layer is lighter than the rest of the contrast substance, and of an ashy color. This secretion layer is normally only seen in the beginning of digestion. In some cases no secretion layer is seen during any part of digestion.



*Intermediary layer due to hypersecretion*

FIG. 8

4. MODE OF FILLING AND MOTILITY. An understanding of the mode of filling of the normal stomach, as well as the time of emptying under normal conditions, is essential in order to judge it intelligently in pathological conditions. The stomach in an empty state represents a narrow sausage-shaped tube, with lesser and greater curvature separated from each other. This was conclusively proved by the ingenious experiment of Groedel, who fastened silver pearls along both curvatures of the stomach of a dog in order to make the outlines of the stomach visible to roentgen rays. At the top of this narrow tube, just under the diaphragm, air is seen (air-bag or *magenblase*). When food is taken the filling of the normal stomach occurs in the following manner: The first morsel reaching the fundus (*fornix*) stops just below the air-bag (Fig. 9a) for an appreciable time, three to five seconds. It then slides downward, forming a triangle with its base upward (Fig. 9b). Then it is seen in an elongated sausage-shaped form (Fig. 9c), finally reaching the caudal point (Fig. 9d). This entire procedure occurs along the lesser curvature in the groove of Retzius, termed "*magenstrasse*" (road to the stomach). The successive morsels follow the same road until about five tablespoonfuls are taken, when the stomach is seen filled in its entire form from the fundus to the pylorus. The rest of the meal, or 500 grams, distends the stomach in width but not in length.

The emptying time for the Reider meal under absolutely normal conditions has been estimated by most authorities to be between three to six hours. When food is given with barium instead of

bismuth, emptying is hastened by one hour. We use a more substantial meal consisting of 400 grams buttermilk, 80 grams barium sulphate. Two soft-boiled eggs, and 50 grams buttered white bread. After such a meal we invariably find the stomach empty in six hours in absolutely normal individuals. The bull-horn type empties sooner than the siphon type.

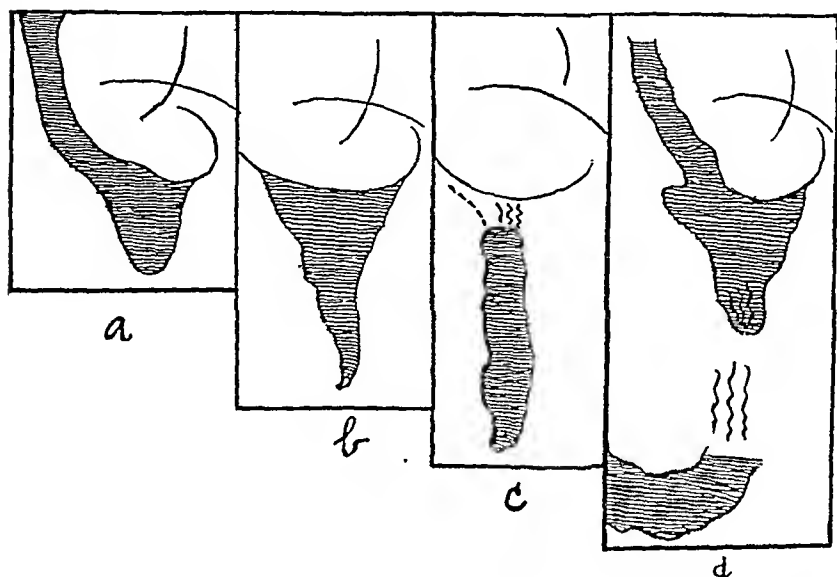


FIG. 9.—a, first morsel; b, triangle; c, sausage shaped; d, caudal part. (Groedel.)

5. **MOBILITY.** Normally, the entire stomach moves upward with inspiration and downward with expiration. With the palpating hand or by a Holzknicht distinctior one can displace a normal stomach in all directions. The bull-horn-shaped stomach is not as freely movable as the siphon form. Exaggerated mobility is seen in individuals with status asthenicus. A siphon-form stomach moves up to three to five inches, with the patient in the horizontal position. The bull-horn stomach moves up very little in the horizontal position, mostly from one-half to two inches.

Having briefly discussed the roentgen-ray physiology of the stomach we are more nearly ready to interpret the importance of deviation from the normal, upon which diagnosis of simple and complicated ulcer is so greatly dependent.

In the roentgen-ray diagnosis of a simple ulcer the indirect method should afford a means in the majority of cases for determining the existence of an ulcer as well as its localization. Hyperacidity and hypersecretion, being the main functional disturbances in ulcer simplex, are largely responsible for the roentgen-ray manifestations. The same functional disturbances, however, express them-

selves roentgenologically differently, depending on the underlying tone of the stomach. Hence our interpretation must be guided by the fact whether we are dealing with an ortho-, hypo-, or hypertonic stomach. Our roentgen-ray observation in ulcer simplex, independent of the tone of the stomach, must be directed to the following cardinal points:

1. Mode of filling, position, and peristalsis.
2. Sensitive pressure points.
3. Secretions.
4. Standing contraction (persisting contraction).
5. Time of emptying.

1. **MODE OF FILLING, POSITION AND PERISTALSIS.** With these points in mind our roentgen-ray observations of the simple florid ulcer in an orthotonic stomach are the following: The organ fills slowly, the food staying in the fornix longer than usual. The entire stomach distends slowly as the food comes down, and peristalsis throughout the organ, from incisura cardiaca to pylorus, is almost instantaneous. The period of repose is shortened or even missing.

The peristaltic waves even in the tube are usually deep, and especially so in the sinus, so that at the beginning of the vestibule the waves deepen to such an extent that the stomach appears divided into two compartments. The peristaltic waves are of a lasting and standing nature, indicating that normal contraction waves are here converted into a state of spastic contraction. The number of peristaltic waves to each minute is diminished.

Because of such marked contractions the stomach has more of a transverse appearance, with the sinus and pylorus to the right of the median line, which also makes the pylorus appear to be the lowest part of the stomach. The vestibule (pylorus) is closed, indicating the existing spasticity; whatever food passes through the sphincter is seen in a very thin stream (goose feather); even the first portion of the duodenum is not completely filled and the small intestine fills very slowly. Later in the course of digestion one sees peristalsis less active than in the beginning, probably due to exhaustion of the musculature, but the pylorospasm still persists.

The mode of filling and peristalsis thus described is observed independent of the seat of the ulcer.

Secretion, standing contraction, and time of emptying will often indicate not only that an ulcer exists but even its location.

2. **SENSITIVE PRESSURE POINT.** Jonas and Jolasse laid considerable stress on the diagnostic importance of sensitive pressure-point in ulcer of the stomach in determining the existence as well as the seat of ulcer. According to these authors the sensitive pressure-point is movable with the mobility of the stomach brought about by respiration, etc. In simple ulcer no importance can be attached to this phenomenon. In complicated ulcer, to be described later, the sensitive pressure-point is of greater significance.



3. SECRETION. The intermediary layer of Schlesinger indicating the existence of secretions, as stated above, is normally very small in the ortho- or hypertonic stomach. A large intermediary layer in such organs indicates the existence of a hypersecretion, due, in the majority of cases, to ulcer ventriculi or ulcer duodeni. We have observed in a number of cases that the secretion layer is most marked in that part of the stomach nearest to the ulcer. If the ulcer is near the cardia the layer of secretion is most marked in the fornix. If, on the other hand, the ulcer is in the tube, pylorus or sinus the corresponding regions are seen to contain the most secretions. We see, therefore, that a close study of the part of the stomach in which the secretions are most abundant may lead us to a proper localization of the ulcer.



FIG. 10.—X-ray. Hour-glass contraction. Not persistent.

4. STANDING CONTRACTION (incisura; spastic or intermittent hour-glass contraction). Standing contraction manifests itself as an indentation on the greater curvature in the region of the tube (Fig. 10). It is due to a spastic contraction of the circular muscle fibers in the plane of the ulcer. The width of the incisura is greater the larger the ulcer. This incisura persists during the entire course of digestion and seldom relaxes on the administration of atropin, tincture of belladonna or papaverin, and it can be demonstrated during repeated examinations so long as the ulcer is in a florid state. Only deep narcosis causes relaxation of the spasm and makes the incisura disappear, hence it is not demonstrable on the operating table.

The incisura, such a valuable sign in ulcer of the lesser curvature, is at times encountered in extragastric conditions (of extrinsic nature—Carman). Hirst, of London, was the first to show that pressure over the region of a chronic appendix brings about such an indentation. Baron and Barsoni, as well as Case, produced a similar

indentation by exercising pressure over the right hypochondrium in duodenal ulcer, and Carman found the same in gall-stones.

According to our experience the findings of these authors are met with very rarely, and if present at all are found only in ortho- or hypertonic individuals, and where gastric symptoms are quite prominent. The indentation is of a very transient nature. Removal of the palpating hand makes the indentation disappear. According to Carman these indentations are of extrinsic origin because no ulcer can be demonstrated at operation. It is well known, however, that the surgical diagnosis at the operating table is founded on palpation of the ulcer. Only rarely is the surgeon tempted to open the stomach and look for the ulcer. From postmortem studies it is known that scars of healed gastric ulcers are very frequently found. Roessle, who studied the etiology of gastric ulcer in relation to extragastric affections (appendicitis, gall-stones, etc.), found signs of healed gastric ulcer in a great number of cases. He accordingly termed the ulcer of the stomach a secondary affection.

From Roessle's studies as well as from our own clinical observation we are led to believe that even the transient incisura is an expression of an erosion or superficial ulcer on the lesser curvature which cannot be demonstrated at operation and heals when the etiological factor is removed. Our conviction is strengthened by the clinical observation that hematemesis may result from an appendix or diseased gall-bladder. As we know that the theory of the embolic bleeding from the stomach (Eiselsberg) does not hold it is reasonable to conclude that an eroded vessel of the ulcerated area is the cause of the bleeding, although the ulcer is so superficial that it cannot be demonstrated at operation.

It is of practical importance, when a transient incisura is found apparently of extrinsic nature, to urge the removal of the cause in order to prevent the formation of a chronic ulcer.

Incisuræ are likewise met with in individuals of a vagotonic type who have an ortho- or hypertonic stomach. Such an incisura disappears on the administration of atropin or atropapaverin or tincture of belladonna administered according to the method of Carman—*i. e.*, 10 drops, three times a day, two or three days before the examination. Its extrinsic nature is demonstrated by the non-persistence of the incisura; here again we must remember that in the vagotonic incisura, although transient, von Bergman proved the existence of a real ulcer (spasmogenic ulcer). It is therefore safer in vagotonia when an indentation is demonstrable to give the patient the benefit of the doubt and treat for ulcer.

Pressure from without (enlarged spleen, gas or tumor of the splenic flexure, etc.) on a stomach with good tone may produce an incisura. Differentiation is accomplished by palpating the abdomen in the course of fluoroscopy, thereby detecting the extragastric origin.

Carman called attention to the spastic contraction on the greater

curvature with a carcinoma of the lesser curvature. According to his view the width of the incisura is more extensive and the lesser curvature stretched out and stiff. Le Wald, Carman, Case and others described cases in which a typical spastic hour-glass contraction was due to syphilis of the stomach.

Analogous to the indentation in the region of the tube which, as shown above, is an expression of a spastic contraction of the circular fibers are the spastic contractions taking place at the cardia and pylorus if an ulcer is situated in those respective regions. If the florid ulcer is near the cardia, cardiospasm results. The entrance of the food into the stomach is hindered and the food accumulates in the esophagus above the cardia, causing a spindle-shaped dilatation of part of the entire esophagus. Either no food at all or a very thin stream of food is seen to pass through the spastic cardia.

Although cardiospasm is a very valuable sign of ulcer near the cardia it must be remembered that a number of other conditions (vagotonia, gall-stones, uremia, etc.) may cause the same condition. Only in combination with other clinical signs and symptoms of ulcer can cardiospasm be considered in the localization of the ulcer.

In order to utilize pylorospasm in localizing an ulcer we must take into account whether the spasm is confined to the sphincter pylori or involves the entire vestibule. A spasm at the sphincter manifesting itself as an abruptly cut-off pylorus, where no food is seen to pass into the duodenum for many minutes and then only in the form of a very thin stream, signifies ulcer at pyloricum. A spasm of the vestibule (pylorus proper) manifesting itself as a spigot-like tube, points to the seat of the ulcer as being aproximal to the sphincter proper. We therefore prefer to differentiate between spasm of sphincter and spasm of pylorus proper.

A spasm of the sphincter pylori may be of a reflex nature, with an ulcer on the lesser curvature of the stomach or of extragastric origin (vagotonia, chronic appendicitis, gall-stones, gastric crises, and in most acute intra-abdominal disease).

Only in combination with other clinical data of ulcer does spasm of sphincter pylori speak for ulcer ad pyloricum. By pylorospasm we understand a spastic contraction of the entire vestibule (antrum pylori). The pylorus appears elongated and contracted (spigot form). In contradistinction to spasm of the sphincter pylori food is seen to pass continually in a width corresponding to the contracted pylorus. The first portion of the duodenum (bulbus duodeni) is never seen completely filled.

A spasm confined to the vestibule only, indicates in most cases ulcer proximal to the sphincter. Unlike spasm of the sphincter pylori, spasm of the entire vestibule is but seldom of extragastric nature.

Sometimes the spasm may involve larger areas of the stomach sinus and pylorus in cases of ulcer of the stomach. We then have

the picture of a tube-like sinus and pylorus and a large sac-like tube and fornix. Such a stomach simulates strongly a carcinoma of the sinus and pylorus. The differentiating points are that the pyloric sphincter in carcinoma is open, the defect is irregular, and in most cases corresponds to a palpable tumor. Very seldom does one meet with a spastic contraction of the entire stomach (gastrospasm) in cases of *ulcus ventriculi*. The entire organ then looks like a tube simulating scirrhus carcinoma of the entire stomach. Such a stomach empties quickly. It must be mentioned, however, that spasm of sinus pylorus or gastrospasm is most frequently of extragastric origin (morphin, nicotin or lead-poisoning, gastric crisis, cholelithiasis).

Huerter, through whose kindness we are enabled to publish Fig. 11, was the first to show that a small local spasm may be met with just as the seat of the ulcer.

In certain cases the spastic contraction of the pylorus manifests itself in irregularities with teeth-like indentations in the pylorus; the above-named changes in the pylorus are not due to adhesions but are the result of spastic contractions.



FIG. 11

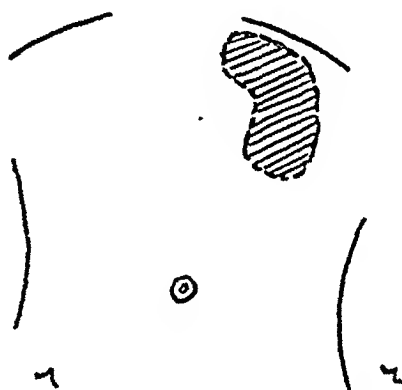


FIG. 12.—Kidney-shaped stomach.

To the localization of ulcer Schmieden contributed considerably when he described the snail or tobacco-pouch stomach. This stomach, as shown in Fig. 12, is usually situated high in the abdominal cavity, the pylorus and cardia so near to each other that but little is seen of the lesser curvature. The stomach is almost entirely to the left of the median line, and is smaller than the average stomach. Schmieden attributes this configuration to the excessive contraction of the longitudinal musculature, the result of an ulcer of the lesser curvature. The findings of Schmieden were confirmed by other observers.

His belief that the tobacco-pouch stomach is characteristic only of ulcer at the lesser curvature, and is the result of an ulcer penetrating directly into longitudinal muscle, does not correspond to our experience. We found that this form, even with ulcer of the

lesser curvature, is only present at the time when the subjective disturbances due to ulcer are pronounced, proving the functional nature of the deformity. Besides that such a snail-form stomach may be the result of extragastric influences.

If pressure from without—such as gas or tumor in the splenic flexure, tumor of the pancreas—is exerted on the stomach musculature of normal tone an organ of the tobacco-pouch shape may result.

We see therefore that useful as is this form of stomach in diagnosis and localization of gastric ulcer it will lead to mistake if we base our diagnosis on the roentgen-ray findings alone.

5. TIME OF EMPTYING. The time of emptying after a standard meal as mentioned above, when barium sulphate is used as a contrast substance, is from two and a half to four hours, and when bismuth subcarbonate is given, from four to five hours. Six hours is the maximum time of emptying.

Some authorities have objected to accepting the roentgen rays as a determining method for the emptying time, asserting that the contrast substance may hasten the emptying in some cases and retard it in others independent of disease. Bassler even obtained contents with the stomach tube in individuals in whom no roentgen-ray residue was visible. We concede the above possibilities, with the exception that under perfectly normal conditions the vast number of cases already studied by roentgen rays throughout the world demonstrate that a normal organ empties itself of a standard meal within six hours and residues demand an explanation.

Haudek and Clairmont laid down a definite rule that when a florid ulcer of the stomach is present there is in every case a six hours' residue. Roentgenologists of large clinics, notably Faulhaber, von Bergman, Case, Carman, Hirsch and others contradict the assertions of Haudek. Faulhaber formulated the rule that a six hours' residue is only present when a florid ulcer is situated at the pylorus; if, on the other hand, the ulcer is situated proximally to the pylorus there is no six hours' residue.

That the assertion of Haudek cannot be taken as absolute is proved by the fact that clinicians like Riegel, Boas, Ewald, Strauss, L. Bamberger and others who studied extensively the influence of ulcer ventriculi on time of emptying would have found by their exact methods a delay in emptying pathognomonic of ulcer ventriculi. In reality, however, this was not the case.

The findings of Haudek must therefore be attributed to three factors: (1) that most of the cases studied by him were complicated surgical ulcers; (2) Haudek allowed food between the six-hour periods; (3) he does not specify the existing tone of the stomach where residues were found. Faulhaber's assertions are far more applicable in the greater number of cases, but they are dogmatic and lack explanation.

From experiences obtained thus far we agree with von Bergman that a six hours' residue is most often present when a florid ulcer is situated at the pylorus, and in a lesser number of cases a residue is present even in an ulcer situated proximally from the pylorus, although the organ is of good tone.

Continental roentgen-ray men made the correct observation that location of the residue often indicated the seat of the ulcer. When the ulcer is at the pylorus the residue is more in the pyloric region, while an ulcer in the region of the tube shows the residue in that location. It is also worthy of mention that florid pyloric (sinus) ulcers give large residues which sometimes extend to twelve hours. Such residues often simulate organic stenosis, and only atropin or atropapaverin or the subsidence of the florid state show that the residue was due to a prolonged spasm of the sphincter pylori.

With an ulcer on the lesser curvature in the region of the tube, if residues are present at all they are usually small. In a pyloric ulcer the residue is easily explained by the spasm of the sphincter pylori brought on by the continuous hypersecretion. When the ulcer is in the region of the tube the reflex spasm is only present during the first hours of digestion, as long as considerable quantities of food are still transported from tube to sinus. After that the cause of irritation is removed, both local spasm (standing contraction) and reflex pylorospasm are removed and the stomach empties itself on time. In a smaller number of cases the local ulcer causes enough hypersecretion to bring about a more persistent local spasm. Here we find a small residue situated to the left of the median line which consists chiefly of secretions and contrast substance. Clinically, such patients have pains from one-half to one hour after meals, lasting until regurgitation or vomiting of the excessive secretions brings relief. The six hours' residue is of substantial diagnostic importance in pyloric ulcer.

As a matter of fact, however, six hours' residues are at times found in the stomach not the seat of an ulcer. This should not discredit its diagnostic importance if the distribution of the contrast substance throughout the intestines is taken into consideration in connection with the residue in the stomach.

In simple ulcer of the stomach the small intestines show six hours after the meal, but very little contrast substance. This is due to the fact that the excessive secretion and peristalsis of the stomach brings about thorough chymification and digestion, so that the digestion in, as well as the motility of the small intestine is hastened.

If in six hours after a meal a residue is found in the stomach accompanied by an overfilling of the small intestines with contrast substance it is usually of extragastric origin.

The most frequent causes are atony of the stomach of extra-

gastric origin (status asthenicus, wasting diseases, old age, etc.) and achylia gastrica without hypermotility of the intestines. In both cases the deficient digestion of the food in the stomach necessitates a prolonged stay of the food in the small intestines for vicarious digestion, thereby retarding the emptying of the stomach.

A small residue in the stomach characteristic of duodenal ulcer, or gall-stones with duodenal irritations, or adhesions around the duodenum is, according to our opinion, which we have repeatedly demonstrated by the stomach tube, due to the gastric secretions holding the contrast substance in suspension, and it in reality therefore only simulates a residue.

**ULCUS SIMPLEX IN A HYPOTONIC STOMACH.** The roentgen-ray manifestations brought about by the hypersecretion and hyperacidity resulting from the ulcer are somewhat different in the hypotonic stomach than the hypertonic stomach. In diagnosis of ulcer ventriculi in the hypotonic stomach it is also best to direct our attention to the following cardinal points: mode of filling, position of the stomach, peristalsis, sensitive pressure-point, secretions, standing contraction, and time of emptying.

The mode of filling in the hypotonic stomach without an ulcer is as follows: the food is seen to drop down to the caudal point, the stomach filling itself from below upward. Most of the food is seen in the sinus and pylorus; while the tube contains but little food, the fornix (sac) is made up of a large pear-shaped air-bag.

The position of the hypotonic stomach when the seat of a florid ulcer differs from the non-diseased hypotonic stomach, inasmuch as the sinus and pylorus are considerably to the right of the median line (for comparison see Figs. 13 and 14), so that the pylorus is lower than the normal hypotonic stomach and early in the filling process, before peristalsis sets in, the sinus and pylorus give the impression of a half-moon or boat-shaped organ.

Peristalsis begins earlier than in the normal hypotonic stomach. Whatever is visualized of the tube shows but very superficial peristalsis, while in the sinus and pylorus peristalsis is so deep that the stomach is seen separated into two or three globe-shaped compartments. Because of the excessive contractions the stomach appears shorter. The intensity and duration of the peristaltic waves due to the underlying weakened tone of the musculature is only transient. Secretions are usually very marked; they are seen to fill the tube and even sinus and pylorus. Sensitive pressure-points have very little value in simple ulcer in general, especially so in hypersensitive individuals.

The standing contraction discussed above, which is of such value in the localization of ulcer in the ortho- or hypertonic stomach, cannot be utilized to such an extent in the hypotonic individual. This is primarily due to the weakened musculature of the tube. In a number of cases, even in a hypotonic stomach, the standing

contraction can be brought about when the patient is examined in a horizontal position. The standing contraction is only to be utilized as pathognomonic of ulcer of the lesser curvature in case it persists when the patient is examined on his back, abdomen, or on his right side. This will help us to rule out a standing contraction brought about by pressure from without.

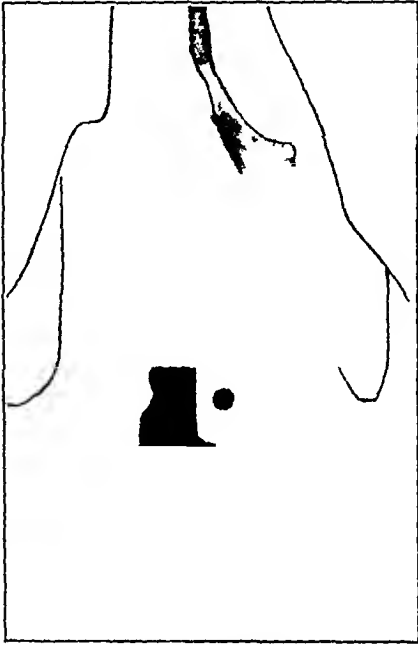


FIG. 13.—Hypotony.

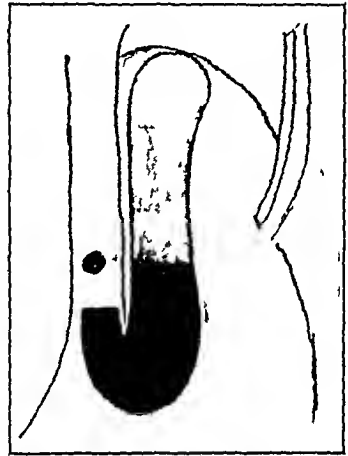


FIG. 14

While the standing wave is of but little value in the hypotonic stomach the spastic contractions at either end of the stomach (cardia or vestibule) are of great aid in the diagnosis and localization of ulcer. If the ulcer is at the cardia the associated cardio-spasm with the characteristics described above are met with. In the hypotonic stomach the interpretation as to whether the cardio-spasm is the result of traction on the esophagus or because of an ulcer will depend on the knowledge of the entire clinical picture.

If the ulcer is at the pylorus, spasm of the sphincter pylori results.

Time of emptying in the hypotonic stomach is moderately delayed even in a normal individual, but after six hours the hypotonic stomach, not the seat of ulcer, is empty. If an ulcer is present the six hours' residue is only present when the ulcer is in the vicinity of the sinus or pylorus, demonstrating again that the residue is the result of the existing spasm of the sphincter. It was pointed out by Kreutzfuchs that a hypotonic stomach with pyloric ulcer shows smaller residues than a hypertonic stomach. The same author attributed this to the fact that spasm of the sphincter pylori in the hypotonic stomach is not so persistent and lasting as in the hypertonic stomach.



**DIFFERENTIAL DIAGNOSIS.** We have attempted to show that by means of the indirect method one can, depending on the functional disturbances caused by the ulcer, obtain definite roentgen-ray data as to the existence and seat of a simple ulcer. We have also shown that the roentgen-ray manifestations in individuals with ortho- or hypertonic stomachs are different from those in individuals with a hypotonic organ, because the functional disturbances caused by the ulcer are not alike in both types. It is clinically known that a great many chronic intra-abdominal diseases of extragastric origin, as well as functional and organic nervous diseases, cause gastric symptoms simulating ulcer. As these symptoms are dependent on disturbed gastric function (hyperacidity, hypersecretion, etc.) it might be supposed that the roentgen-ray findings of the stomach would, to a great extent, likewise simulate ulcer. While such a supposition is in a certain number of cases correct, and a differential diagnosis impossible; it will be shown that in a great number of cases the roentgen-ray findings furnish an important additional link in the establishment of an exact diagnosis.

It is self-evident that intra-abdominal diseases, like appendicitis, gall-stones, renal colic, etc., which by virtue of the local affection cause corresponding local symptoms, give no rise to diagnostic difficulties and make the roentgen-ray examination of the gastrointestinal tract superfluous. We refer to intra-abdominal diseases of extragastric nature in which the local symptoms are insignificant as compared to the reflex gastric symptoms. Such diseases may manifest themselves in the form of either acute or chronic gastric disturbances.

In the state of acute exacerbation, be the cause appendicitis, gall-stones, and tabes dorsalis, or vagotonia, it is, as pointed out by Mayo, the persistent pylorospasm that is responsible for the acute attack. The roentgen-ray manifestations will therefore be those of pyloric ulcer with marked gastric retention.

At operation the real cause of the mere functional nature of the spasm will be found. A number of careful observers, like Levy and Kantor, Levy-Dorn, von Bergman and others, described their experiences of cases which roentgenologically showed marked retention in the stomach and the operation revealed gall-stones, chronic appendicitis, etc. Levy, of Syracuse, is right when he asserts that the mistake is not a serious one so long as a surgical condition is the cause of the symptoms.

It must, however, be mentioned that vagotonia, gastric crises, abdominal vascular crises causing during acute attacks pylorospasm, and gastric retention must be thought of and excluded.

These extragastric diseases after subsidence of the acute symptoms may leave the patient with chronic gastric complaints, such as pyrosis, epigastric pressure, fulness after meals, marked sensitiveness to various articles of food, etc. The gastric symptoms are of

reflex origin and are due to hyperirritability of the stomach. In this state even a normal stimulus causes abnormal sensations. Such an individual therefore is found with secretions quantitatively and chemically normal but with symptoms of hypersecretion and hyperacidity. Should secretions be actually increased the symptoms are aggravated out of proportion. Some cases, although showing a subacidity, will, on account of local hyperirritability, have symptoms of hyperacidity (anacida hyperacida, Strauss).

It is well known to all clinicians how difficult it is to diagnose such cases with exactness. Only too often has the stomach erroneously been accused of being the seat of the disease and quite as frequently a gastric neurosis or other intra-abdominal disease diagnosed when the stomach is the seat of the affection.

Roentgen-ray studies of the gastro-intestinal tract by means of the indirect method have proved a very valuable aid in differential diagnosis. Such functional disturbances as can be visualized by the roentgen rays (hypersecretion, hyperperistalsis, etc.) do not differ from a functional disturbance of the stomach due to ulcer. The vital difference lies in the fact that if an ulcer gives rise to functional disturbances, material interference with the chemical and mechanical action of the stomach results as described above, while in reflex gastric disturbances the functional derangements manifest themselves only in the beginning of digestion, becoming adjusted as digestion continues. On account of such an adjustment there is no delay in the emptying of the stomach. This fact and other points to be mentioned enable us in a fair percentage of cases to localize the seat of the disease.

For roentgen-ray differentiation of ulcer ventriculi from chronic appendicitis simulating ulcer ventriculi the following points are useful:

Individuals with orthotonic stomachs will show characteristics of hypertonicity due to reflex disturbance of the vagus from the chronic appendicitis. This will at first sight give the stomach the roentgen-ray appearance of an ulcer of the stomach. Prolonged fluoroscopy, however, will demonstrate the hyperperistalsis, the spasm of the sphincter pylori, the transversely situated stomach to be only of transient nature. Passage of the food through the pylorus is normal. The observation of Hirst that pressure over the appendix produces an incisura on the greater curvature near the cardia simulating ulcer of the lesser curvature is indeed at times met with, especially in congenital vagotoniacs. This incisura, however, is extraordinarily fleeting. After removal of the hand from the region of the appendix the indentation soon disappears.

Very conclusive is the observation six hours after the contrast meal. The stomach is usually entirely empty, but the small intestine, and especially the ileum, are unusually full. If in addition to this one finds fluoroscopically a fixed cecum the diagnosis of chronic appendicitis is strengthened.

In individuals of the asthenic type, where chronic appendicitis simulates ulcer ventriculi one finds, when the stomach is full, the characteristics of the hypotonic stomach. The most important finding is delay in the ileum. In cases in which vagotonia is a marked factor, even the hypotonic stomach may show hypercontractions of sinus pylorus as in ulcer, but unlike ulcer the hypercontractions are of a very transient nature.

Cholelithiasis with gastric symptoms simulates more often clinically and roentgenologically ulcer duodeni, and therefore is not discussed here.

Individuals of the vagotonic type will clinically and roentgenologically simulate ulcer ventriculi. A differential diagnosis can only be made by repeated examination, demonstrating the instability of findings in spite of existing symptoms. It cannot be emphasized too strongly that vagotonias, as first pointed out by von Bergman, are very often predisposed to ulcer ventriculi.

Individuals with disturbed intermediary metabolism, such as phosphaturia, oxaluria are very frequently subject to gastric symptoms simulating ulcer. Such patients are subject to a long list of general nervous symptoms, including gastric hyperacidity, especially in phosphaturia, and should their attention be diverted by the physician to the hyperacidity, the suggestion that the disease is primarily gastric never leaves them.

The diagnosis rests with complete examination of the urine and the favorable results obtained by properly applied therapeutics. The roentgen ray is of aid inasmuch as negative findings are obtained.

**COMPLICATED ULCER.** If simple ulcers do not progress favorably they may lead either to the ulcer penetrating all the layers of the stomach including serosa as well as adjacent organs, or to excessive connective tissue formation, adhesions, etc. We then speak of complicated ulcer. Here the roentgen ray directly visualizes the existence as well as the seat of the ulcer in the great number of cases.

*Ulcus Callosum.* In long-standing ulcers, as a result of round-cell infiltration and connective-tissue formation at the seat of the ulcer, a callous ulcer results. Roentgenologically this is best demonstrated when situated, as it often is, on the lesser curvature. It is seen as a diverticulum filled with contrast substance (Fig. 15), mostly round, sometimes quadrangular or triangular. Haudek named this diverticulum "niche." When the stomach is quite emptied the diverticulum is likewise empty. Such diverticuli are but seldom situated on the posterior or anterior walls of the stomach. For the visualization of a niche on the posterior or anterior wall, special methods of examination have been suggested. Holzknecht advises that the patient take a contrast suspension while lying on the right side and remain in that position for a few minutes; he should then take the Rieder meal in the sitting position, be fluoroscoped, and a plate taken in the standing position. To render a

diverticulum visible on the posterior wall, Schwartz advises that the patient take the bismuth suspension while on his back and remain in that position for a few minutes, then sit up and take the Rieder meal, then be fluoroscoped and a plate taken in the ventro-dorsal position (front to tube and back to screen). For a niche on the anterior wall it is best to fluoroscope and take a plate with the patient lying face downward.

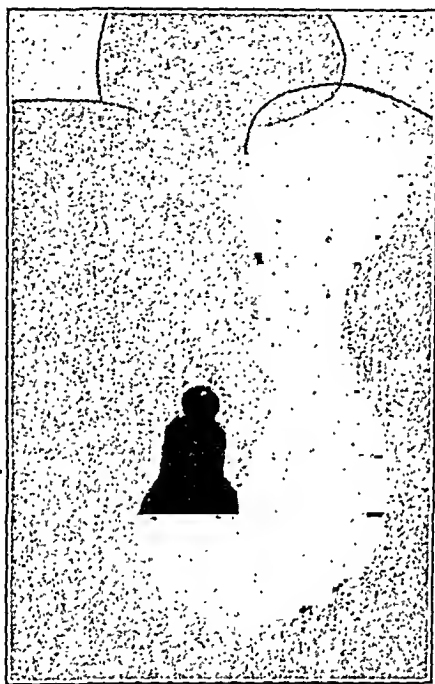


FIG. 15.—Ulcer callosum of small curvature.

Two conditions which may simulate the picture of niche are: the presence of contrast substance in a loop of small intestine which happens to overlay the lesser curvature, and calcareous glands in the region of the lesser curvature. Cole recently expressed the view that such a diverticulum signifies in the majority of cases carcinomatous degeneration of the ulcer. This was emphatically contradicted by I. S. Hirsch. From our own experience we agree with Hirsch, Haudek and others that a niche does not signify malignant degeneration.

Cole in this connection creates a new term—"indurative" ulcer. He defines an ulcer as indurative when surrounded by an amount of exudate reaching the muscular coat, so that the ulcer can be palpated during surgical procedure or necropsy. By his direct method of visualization by serial radiography, he diagnoses the existence of such an ulcer by the absence of peristalsis in that particular part so that the area appears to be stretched out. The indurated ulcer he considers as a stage preceding the callous ulcer.

He therefore strongly emphasizes the importance of recognizing an indurated ulcer so as to prevent the occurrence of a callous ulcer, which he considers analogous to a carcinomatous degeneration of the ulcer.

In the same article Cole publishes cases not at all corresponding to his definition. For instance, in the case operated by Deaver the ulcer could neither be seen nor palpated until the stomach was opened, and still when Cole examined that case before operation he claims to have found roentgen-ray evidence of threatening perforation. Another of his cases, in which he shows the straight line on the lesser curvature corresponding to the indurated area, proved at the operation to be due to adhesions. A number of his other photographs show ordinary niches.

Our conclusions cannot be modified by his article, and we believe that a stretched-out or stiff lesser curvature is the result of adhesions, or as Levy-Dorn has pointed out, small carcinoma on the lesser curvature. Real marked indurations manifest themselves as niches (Haudek).

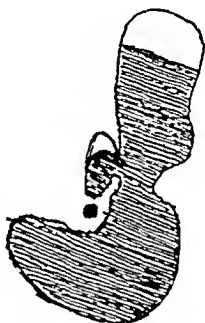


FIG. 16.—Penetrating ulcer.

**ULCUS PENETRANS.** We speak of penetrating ulcer when repeated small perforations have taken place, resulting in adhesions between the ulcer and the neighboring organs. These adhesions are mostly found between the stomach and the liver or pancreas. The penetrating ulcer manifests itself as a niche filled with contrast substance on top of which a small air-bag is seen (Fig. 16). This niche and air-bag are seen after the stomach has emptied itself.

Penetrating ulcers on the posterior wall of the stomach are localized by examining the patient in a ventrodorsal position. From the description it is evident that we must not confuse callous ulcer with penetrating ulcer. From our studies we have reason to believe that the callous ulcer, especially of the lesser curvature, is mostly present in an ortho- or hypertonic stomach, while a penetrating ulcer of the lesser curvature is found in the hypotonic stomach. With a callous ulcer on the lesser curvature there is often a small standing contraction opposite the seat of the ulcer, while in

a penetrating ulcer the region of the stomach corresponding to the seat of penetration is only seen in the form of a small streak of contrast substance with accumulation of contrast in the cardia above and the sinus-pylorus below. Such a stomach simulates an organic hour-glass contraction.

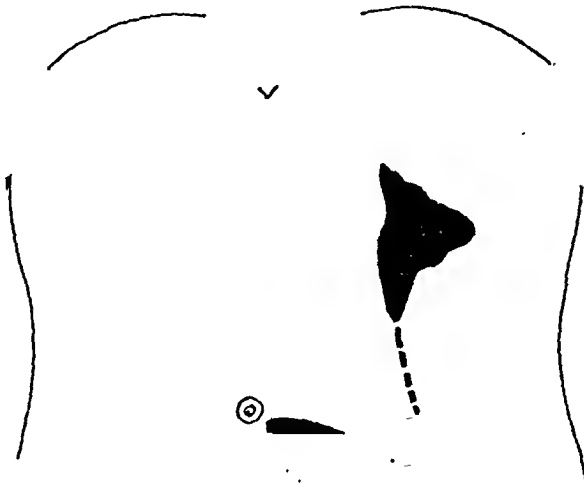


FIG. 17.—Hour-glass contraction of the stomach.

**ORGANIC HOUR-GLASS STOMACH DUE TO ULCER.** This stomach results when excessive connective-tissue formation divides the stomach into two compartments. The roentgen-ray manifestations of such a stomach (Figs. 17 and 18) are the following:

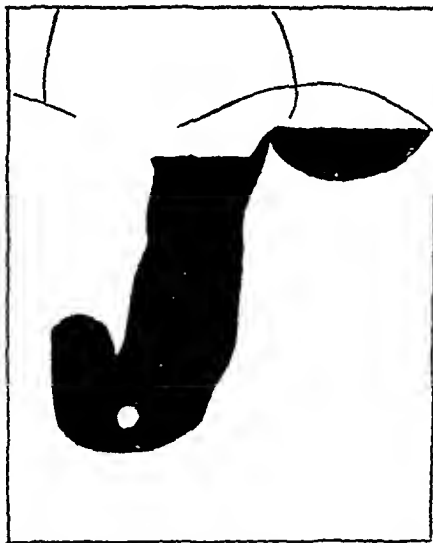


FIG. 18.—Rare form of hour-glass stomach. (From Faulhaber; Roentgen-diagnostic d. Nagenkrankheiten.)

When the contrast food is taken only the cardia fills, forming a round ball lying directly under the diaphragm. From time to time

only a string of contrast substance is seen to dribble down to the lower compartment forming two distinct portions.

There are a few other affections of the stomach which may simulate hour-glass contraction—carcinoma of the greater curvature in the region of the tube at times gives such a complete defect that the stomach looks subdivided into two compartments connected by a narrow band. In carcinoma, however, the intervening space between the two sacs has an eaten-out appearance corresponding to a distinct defect in filling. The connecting link between the two sacs is wider and corresponds to the lesser curvature. Fluoroscopically one sees such a stomach fill in both sacs simultaneously because of the food dropping down through the involved part very readily. Palpation in the course of fluoroscopy will disclose a palpable mass corresponding to the region of the defect.

*Syphilitic gumma of the stomach*, as pointed out by Le Wald, may simulate an hour-glass stomach but the intermediary zone likewise shows irregularity and has more the characteristics of carcinomatous hour-glass contraction. Syphilitic gumma of the stomach is rare and the serological examination as well as the therapeutic test will clear up the diagnosis.

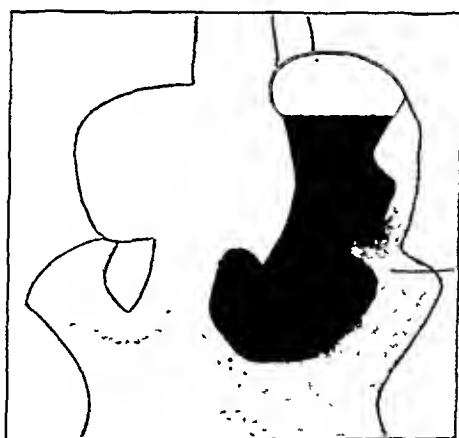


FIG. 19.—Gas in splenic flexure simulating hour-glass contraction.

Tumors of neighboring organs or enlarged spleen as well as gas in the splenic flexure may exercise pressure on the tube of the stomach, causing such an active contraction of the greater curvature (Fig. 19) as to simulate hour-glass contraction. In such an organ the filling is almost normal, but when the stomach is entirely full the narrowing of the tube becomes more distinct, due to the strong contraction of that part. Such a stomach appears shorter and sinus-pylorus to the right of the median line.

COMPLICATED ULCER IN THE REGION OF THE VESTIBULE. A callous ulcer in the region of the pylorus results in stenosis of

various degrees, depending upon whether the pylorus is incompletely or completely occluded. With incomplete obstruction one sees the elongated pylorus without any activity. Even the entrance into the vestibule shows no marked indentation. Peristalsis in the sinus and high up in the tube is increased; whatever food passes the pylorus is seen in a very thin stream. The six-hour residue is very large, due both to the organic stenosis and associated spasm of the sphincter. Residues may extend to twelve and even twenty-four hours. If obstruction is complete the characteristic half-moon-shaped or boat-shaped organ results. Such a stomach never empties in contradistinction to a similarly shaped hypotonic stomach that is sometimes encountered with an ulcer of the pylorus (Fig. 19).



FIG. 20.—Light zone described by Brügel due to callous ulcer in the lower part of pylorus.

A deep-seated ulcer, or adhesions at the pars pylorica, is characterized, according to Brügel, by a horizontal, light, prepyloric zone between the contrast meal above and the pyloric part below. It is requisite that repeated examination shall confirm this finding. Not infrequently pyloric ulcer is complicated by extensive peripyloric adhesions, which manifest themselves roentgenologically by irregularities of the pylorus, stretching of the pylorus to the right of the median line, inability of the pylorus to act with respiratory movements. With marked adhesion the sensitive pressure-point corresponding to the area of adhesions is often very marked. Extensive adhesions posteriorly give the stomach the appearance described by the anatomists, *i. e.*, a transversely high situated stomach with restricted mobility and very superficial peristalsis.



# WAR MEDICINE

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## VINCENT'S ANGINA INFECTION: ITS PREVALENCE, VARIED MANIFESTATIONS, TREATMENT, AND BACTERIOLOGY.

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THE reported frequency of Vincent's angina among the Allied troops serving in France makes a consideration of this malady, and a note or two concerning its bacteriology and treatment, of interest to all concerned with the health of our own men, of whom so many will soon be serving under like conditions. Taylor and McKinstry<sup>1</sup> reported that "during the last few months" over 300 cases of the malady had been confirmed bacteriologically in the Queen Alexandra Military Hospital

<sup>1</sup> British Med. Jour., March 31, 1917, p. 421.

and that "constant presence of these organisms" (the fusiform bacillus and spirillum) had been "abundantly verified" in all forms of ulceromembranous inflammation of the mouth, either alone or associated with various forms of cocci, bacilli and leptothrices.<sup>2</sup>

The last-named observers report that cases of the disease, when affecting the gum margins, were often confused with pyorrhea alveolaris, although pus is usually not produced.

Bouty<sup>3</sup> states: "During the last two years there has been a gradual and marked increase in the number of cases of Vincent's angina among the troops in France, both British and French. In time of peace this disease forms about 2 or 3 per cent. of all cases of throat complaints among the French army (recent statistics). Recent statistics from a British military hospital in France show the proportion to be as high as 23 per cent. of all throat complaints."

Campbell and Dyas<sup>4</sup> reported that during the four months from October, 1916, to February, 1917, 129 cases of the disease had been treated in the Canadian military hospital at Bramshott, England.

*Prevalence in the United States.* I know of no statistics that would show the extent of the prevalence of the disease in this country. It has not been made reportable by any health department, and, short of this or a bacteriological examination of a large number of diseased mouths, throats, etc., in various localities, nothing exact could be known.

The literature dealing with the malady is not great, but there are sufficient reports to indicate that the malady is of universal distribution, although severe cases are not very common under normal conditions in civil practice. However, from the British experience aforementioned, we may anticipate a greatly increased incidence under military conditions.

Among civilians during the last few months I have noticed an apparent increase in the number of tonsillar and pharyngeal sinears, met with both in hospital and private practice, even over the usually increased winter incidence, that show the fusiform spirilliform organisms identified with the condition. Here it may be mentioned that, under the procedures in use at present, in order to make a laboratory diagnosis of the condition a smear and not only a culture is required, the latter alone being sometimes sent for diagnosis.

*Predisposing Causes.* While general debilitating conditions, such as extreme fatigue, chilling, insufficient or improper food, excessive alcohol consumption or the presence of other debilitating disease, undoubtedly markedly influence the incidence of the infection of Vincent's angina, locally acting influences are known to be often determining. Among these are decayed, broken or dirty teeth and excessive smoking or chewing of tobacco.

*Exciting Cause.* This is undoubtedly the organism so constantly associated with the lesions, and which will be considered in detail under Bacteriology.

*Location and Appearance of Lesions.* The typical lesion consists of a heavy, dirty-looking membrane commonly covering one of the tonsils,

<sup>2</sup> Emrys-Roberts, British Med. Jour., September 15, 1917.

<sup>3</sup> British Med. Jour., November 24, 1917.

<sup>4</sup> Jour. Am. Med. Assn., June 2, 1917, p. 1596.

although it may be located any place upon the nasopharyngeal or buccal mucous membrane. It may even extend as a single membrane over most of the surface of the upper respiratory tract, as it did in one of the cases reported in this article. When the membrane is upon the tonsil it commonly either shows a crater-like excavated center or is so necrotic that slight pressure, as with the end of a platinum loop, breaks through and the probe sinks in a half-inch or more. The ulcerations of the disease often cause considerable destruction of tissue and consequent scarring.

Apart from the typical lesions, as described, we must recognize pathological processes of less severity, and which are consequently, less apt to be noticed. Such usually consist of moderate tonsillitis or gingivitis, which has a tendency to chronicity, with now and again a severe attack with lesions of the type first described. An interesting case of this character is detailed in what follows.

In view of the synchronous purpuric manifestations so intimately connected with the throat lesions in the last-mentioned case (see after), and as acute pharyngitis precedes so many cases of purpura, it may be that the specific agent of Vincent's angina has much responsibility for the latter.

Mulholland reported 16 cases of ear infection with Vincent's angina organisms.<sup>5</sup>

Spillman reported a case of gangrene of the vulva and perineum caused by this infection, and Noguchi reported a case of ulcer of the labia due to the same.

Vincent reported several cases of gastro-enteritis in which post-mortem examination showed large numbers of the typical organisms in the intestines.

Ulcerative balanitis due to this organism was described by Corbus and Harris as the "fourth venereal disease." In reporting several cases they declared their belief that this infection was often mistaken for chancroid. The ulcers of the two conditions may resemble each other closely. In chancroids, however, the presence of the causative agent—the Ducrey-Unna bacillus—and the much greater reaction in the buboes, which often suppurate, serve to differentiate.

Bowman<sup>6</sup> reported the case of a soldier with extensive ulceration in the mouth, a severe conjunctivitis and an ulcer on the penis (surrounding the meatus), in all of which lesions the typical organisms were found (Wassermann test negative). Four other cases with penile ulcers due to the same cause were reported by Campbell and Dyas (above).

The latter authorities also reported 7 cases in which a moderately severe bronchitis, with sputum loaded with the typical organisms, was the only lesion.

The writer examined the sputum of a patient (A. H.) suffering from chronic bronchitis in which Vincent's angina organisms were so typical and numerous that he supposed the patient to be suffering from a throat infection, but, upon inquiry, was assured by the attending physician (Dr. O. M. Leiser, New York City) that the lesion was entirely bronchial and pulmonary.

<sup>5</sup> *Annals of Otol., Rhin. and Laryn.*, September, 1915.

<sup>6</sup> *Lancet*, October 6, 1917.

This case was of six months' duration and manifested chronic cough, physical signs of bronchopulmonary catarrh and progressive emaciation; lost thirty pounds. The patient was sent to a tuberculosis sanatorium and, in two months, regained the loss and returned apparently recovered (no tubercle bacilli were ever found in the patient's sputum).

Another case met with by the writer recently was one of nearly daily raising of a small quantity of bronchial mucus on the part of a patient with slight chronic gingivitis. At the time of sputum examination the patient presented a slight ulceration along the inner edge of the under lip. Bronchial mucus, gum margins and lip lesion all showed the typical organisms.

Bouty (see before) reported a recurrence of Vincent's angina on the other tonsil, which was followed in three days by acute nephritis.

In articles on noma, Brault,<sup>7</sup> Herriman<sup>8</sup> and Roma<sup>9</sup> elucidated evidence proving that this malady was caused by the same organism as Vincent's angina and that the difference in the lesions was but one of degree. Vincent<sup>10</sup> considered hospital gangrene a form of the same infection.

*Symptoms and Constitutional Effects (Throat Cases).* These, while directly proportional to the severity of the process, are much less than would be expected from the appearance of the lesions.

Besides the appearances of the involved areas there usually is slight sore throat, headache, malaise, swelling of glands adjoining the ulcerations (in severe cases adenitis is often marked and painful) and a slight elevation of temperature. In severe cases the breath is always fetid. A membrane is usually not formed until the general symptoms have lasted a day or two.

More extensive general manifestations may, however, occur in some cases, as in one detailed herewith, in which nosebleed, gum hemorrhages and general purpuric manifestations seemed to be directly due to the infection. Severe cases reported from the European military hospitals have manifested great prostration, high fever and albuminuria. Recrudescences, as for instance a week or ten days after apparent recovery from an ulcerative process on one tonsil when an ulceration develops upon the soft palate or the other tonsil, have not infrequently occurred.

Several cases (in civilian practice) are recorded in the literature as having terminated fatally. Bouty (above) states that "some cases of death have occurred in French hospitals in which the primary cause was Vincent's angina."

**TWO INTERESTING CASES.** *Case with Extensive Membrane Formation.* C. H., aged twenty-seven years, a lawyer, under the care of Dr. Stephen De Coste, of Brooklyn, after a motor trip to Philadelphia (where he enlisted in the navy), developed a typical membrane covering both tonsils and soft palate, the entire pharynx from the glottis to the posterior nares and extending into both nostrils. The patient said he had suffered from "canker sores" in the mouth for years. The constitutional symptoms were but moderately severe.

On the second day of illness the diagnosis was made bacteriologically and a vaccine of the bacilli prepared. Treatment with the latter was

<sup>7</sup> Bull. Derm. et Syph., 1908, ii.

<sup>8</sup> Arch. Pediat., November, 1905.

<sup>9</sup> Arch. Dermat. u. Syph., 1905, lxxiv, 171.

<sup>10</sup> Deutsch. med. Wchnschr., 1894, xlix, 922.

begun by Dr. De Coste on the fourth day and two doses were given. Before its use, local applications of silver nitrate (10 per cent.) were made, and the case had begun to improve when the specific vaccine was begun. The vaccine was a suspension of 1,000,000,000 bacilli to 1 c.c. The very large first dose of 5 c.c. was followed by a marked local and slight constitutional reaction. Three days later a second dose of 10 c.c. was administered, with like manifestations. The patient rapidly improved, and was well by the tenth day.

*Chronic and Fatal Case.* E. L., aged forty-three years, a physician. Eight years ago E. L. had a chronic ulcer of his nasal septum operated upon, and three days later, besides having had continuous nosebleed in the interval, experienced an attack of general purpura with severe urinary hemorrhage lasting four days (no kidney involvement). Besides also bleeding from the gums and intestinal mucosa the patient's mouth and skin were covered with a small purpuric rash that persisted for several weeks. Since this attack the patient had numerous nosebleeds, gum hemorrhages and purpuric skin eruptions, commonly associated with a tonsillitis which showed as a typical Vincent's angina.

In this connection attention is called to a case (reported by Campbell and Dyas in an article aforementioned), with extensive membrane over the tonsils, entire mouth and lips, which developed an extensive rash four days after admission to the hospital. "The spots, about a dozen on each forearm and leg, were about one-quarter inch in diameter, sharply raised, copper colored, and the center of each contained a small oblong vesicle" (Wassermann negative).

About two months ago the patient (E. L.) suffered an attack which developed a heavy membranous ulceration upon his left tonsil and a general purpuric skin rash. The membrane lasted for about ten days and the rash gradually faded. Smears from the tonsillar membrane showed the typical organism.

As it seemed that the patient suffered from a chronic or recurrent localized infection, I suggested that a vaccine be employed. This was made to contain 1,000,000,000 bacilli to 1 c.c., and a dose of 0.2 c.c. was given ten days after the acute attack described. Within twenty-four hours a rather marked local reaction developed, also a slight bleeding of the gums and nose. At the end of three days the dose was doubled and was followed by a greater local reaction, gum- and nose-bleeding and some purpuric eruptions over the body. Owing to these undesirable consequences, use of the vaccine was suspended, with the intention to resume its use more cautiously as soon as purpuric manifestations subsided.

For a month after the use of the vaccine had been discontinued the patient enjoyed his usual fair health without, however, getting rid of his constant slight chronic gingivitis and nasopharyngeal involvement. At the end of this time he again developed an acute attack, with nasopharyngeal and several small buccal ulcerations. Bleeding was quite marked from the bowels and nose. Temperature was but slightly elevated and the pulse was but a little disturbed. The patient had a moderate bronchitis, with considerable expectoration.

After an illness of four days Dr. Raymond Clark (Brooklyn) was called to attend the patient and requested laboratory tests, which gave results as follows:

*Blood.* Coagulation time (drop method) complete, five minutes; erythrocytes: 3,144,000; size, shape and staining were normal; hemoglobin, 60 per cent.; plaques, 90,000 per cm.; leukocytes, 8800 (neutrophils, 70 per cent.; eosinophils, 1 per cent.; large lymphocytes, 11 per cent.; small lymphocytes, 12 per cent.; large mononuclears, 6 per cent.); culture, negative.

*Feces.* For ova, negative.

*Sputum.* Many typical Vincent's bacilli and spirilla, few or no other organisms.

*Urine.* Negative.

*Smears.* From accessible ulcerations and tonsils showed Vincent's organism to a practical exclusion of others.

At this time the bleeding from the bowels and nose had ceased, but the patient complained of severe frontal headache. For the next three days his condition remained about the same, treatment being directed to relieving his headache. Dr. Clark gave him aspirin for this, and then, when it proved insufficient, codein. At the end of the three days mentioned the patient's head pains had shifted to the left side of the head and neck and extended into the shoulder. They were evidently very severe. On the fourth day of Dr. Clark's attendance (eighth of the attack) the patient rapidly became weaker and died from what Dr. Clark diagnosed as "petechial brain hemorrhage, followed by brain edema."

From the evidence given above it seems reasonable to conclude that Dr. L. died from Vincent's angina infection.

*TREATMENT. Preventive.* It has been reported (Campbell and Dyas above) that 50 per cent. of smears made from the throats of all the troops in a military hospital showed the presence of the organisms of Vincent, so it is evident that the infection must be well-nigh universal. However, before a definite lesion can develop, certain predisposing causes must act. These it is believed have principally, if not entirely, to do with the condition of the teeth and the care given them. The predisposing influences of the irritating effects of tobacco have been mentioned.

Thus it is necessary to have the teeth of all, especially of those entering the military forces, put in the best order possible, and in addition that daily use of the tooth-brush be made.

Excessive use of tobacco should be avoided. Other predisposing conditions to be avoided, if possible, would be, of course, exposure and debility from any cause.

*Curative.* Taylor and McKinstry painted the lesions daily with a solution of salvarsan (strength not given, but presumably quite concentrated). They state:

"When found to be present the peridental gingivitis should be adequately treated as well as the Vincent angina, otherwise the condition is likely to persist indefinitely and to cause repeated recurrence of the sore throat."

Bowman<sup>11</sup> had great success with the following: wine of ipecac,  $\frac{1}{2}$  ounce; glycerin, 1 dram; Fowler's solution, 3 drams—the mixture to

<sup>11</sup> Proc. Roy. Soc. of Med., 1916, ix, 51: and Lancet, October 6, 1917.

be either painted over the lesions or used as a mouth wash, with directions not to swallow any of it.

Emrys-Roberts (above) says that the treatment that has met with unvarying success since its adoption in the area served by his "Mobile Bacteriological Laboratory, B. E. F.," in France, consists in the local application of a lotion composed of hydrogen peroxide, 5 ounces; wine of ipecac, 3 drams; glycerin, 5 drams; water, 2 ounces.

Mercury in any form is stated to aggravate the condition, owing to its well-known injurious effect upon the gums and mucous membranes.

Scargill<sup>12</sup> recommends the "topical application of ordinary tincture of iodine, twice a day." Campbell and Dyas (quoted before) recommended the mouth wash used by Bowman for gingival manifestations, or Fowler's solution alone, swabbed on three or four times a day, for lesions elsewhere. If an ulcer be deep they recommend to paint it once with 10 per cent. silver nitrate solution before beginning the Fowler solution applications. In severe cases the latter recommend salvarsan intravenously or large doses of Fowler's solution internally.

Treatment usually is followed by recovery within a week in the majority of instances.

**BACTERIOLOGY. Lesions.** Smears made from lesions caused by the infection of Vincent's angina show the organisms in a form which varies with the extent of the pathological process. Thus superficial lesions tend to show few or no spirilla, while the bacillus forms are numerous and often varied in shape and size; the typical fusiform bacillus seems to be intermediate between a shorter and a more nondescript shape and the spirilla developments. These latter (the spirilla forms) are seen only in smears made from the deeper ulcerations after some destruction of tissue has occurred.

From the above considerations and the fact that the organism is known to appear as wavy threads among the cells of still living tissue into which it has penetrated,<sup>13</sup> it seems reasonable to conclude that the spirilla forms result from the disintegration of such infected areas. This theory is also borne out by the poor staining quality of the spirilla forms, which would be, as it is, were they old and degenerating. Furthermore, in smears from ulcers caused by the infection we may usually find spirilla linked with fusiform bacilli.

**Cultivation. Morphology.** In a somewhat extended experimentation with organisms from these conditions I have been able to obtain some results previously announced by others as follows:

Tunncliff<sup>14</sup> grew cultures of organism in bacillus form, under anaërobic conditions; transferred plants from such anaërobic cultures and secured growth on Loeffler's solidified blood serum at room temperature; obtained filamentous growth and spirilla forms on this medium.

Noguchi<sup>15</sup> reported that in old cultures, bacillus forms degenerate and often develop larger spherical forms which sometimes appear attached to short forms. It seems to me that these are nothing but the

<sup>12</sup> British Med. Jour., October 6, 1917, p. 469.

<sup>13</sup> This is the case in sections taken from the edge of the still living tissue in cases of noma (see Herman, Arch. Pediat., November, 1905). Tunncliff (quoted elsewhere) grew the Vincent's angina organism from the lesions of noma.

<sup>14</sup> Jour. Infect. Dis., April, 1911.

<sup>15</sup> Jour. Exper. Med., September, 1912.

result of involutionary vacuolization or of the processes common in spore formation (so-called). The granulation process produces forms indistinguishable from cocci.

Campbell and Dyas (quoted before) reported that they found when the organism was "grown anaërobically in aseptic broth containing a piece of tissue—after three or four weeks—a few living spirochetes, very numerous granules and numerous empty shells of spirochetes."

On culture the fusiform bacilli tend to lose their tapering appearance and the spirilla forms ordinarily do not appear. I have noticed that whenever a colony of the bacilli on solidified blood serum produces a digestion of the medium, spiral threads, without septa, are commonly produced, and the same is true of growths on fluid blood-serum media. On this latter, after two or three days' incubation (at 37.5° F.), many of the threads or strings of bacilli will be seen to terminate in a distinct spiral formation, smaller and less distinctly stained than the main portion of the thread. This appearance, when compared with the poor staining of the spiral forms in smears from the lesions and the fact that the spiral forms in the latter are frequently to be seen linked with fusiform bacilli, as previously mentioned, makes it very plain that the two forms—spirilla and fusiform bacilli—are one and the same organism. This belief is well-nigh universal among authorities.

The spiral formation is therefore evidently a degenerating non-septate strand of bacilli, curved in growth, perhaps, and curling more as it shrinks and staining but slightly.<sup>16</sup>

The organism grows under either aërobic or anaërobic conditions, on suitable media, but the activity of any growth varies with the strain, or rather with any peculiarities that it may show at the time experimented with. Such qualities seem to depend upon the immediate ancestry and environmental conditions which acted upon the same. Thus, I have seen a most actively growing culture which formed a thick pellicle upon serum bouillon (and had been cultivated thereon for several generations) fail to grow when a piece of the pellicle was transferred to solidified Loeffler's blood serum.

The organism from C. H., a case reported in this article, when first isolated would not liquefy Loeffler, while that from E. L. (the purpuric case) did. The Loeffler liquefying form shows Gram-positive polar bodies.

The range of temperature at which the organism grows includes "summer heat" (70° F.), so that it is evidently saprophytic.

The culture obtained from the case of E. L., grew well on excised guinea-pig tissue (spleen and kidney), forming a thick pellicle, and penetrating and liquefying the kidneys. In form it was similar to that developing on serum bouillon.

*General Morphology.* The bacilli, in smears from lesions and sometimes from cultures, exhibit, when stained, transverse non-staining bands which vary in number, usually with the length of the organism. Some bacilli, when short and possessing but a single band (bipolar

<sup>16</sup> It should be mentioned, to prevent an impression that such qualities in a bacillus would be unique or extraordinary, that even on artificial cultivation many bacilli show spirilla-like forms—for instance, the *Bacillus lactis albus* (an organism found in milk) produces many distinct spiral forms on nutrient agar.



bacilli), are indistinguishable from diplococci. Some of the spiral forms frequently exhibit similar markings.

The organism when degenerating develops the so-called sporulating form (vacuolization) and granules can be seen escaping from the ends.

The organism is motile, apparently possessing a single terminal flagellum. Unless showing polar bodies (granules) the organism is Gram-negative. When the granules exist they are Gram-positive.

*Animal Experiment.* Bouty reported (see before) that "injection of impure cultures causes abscesses in which the spirochete is abundant."

In a number of trials on two rabbits I failed to produce mouth lesions by the injection of serum-bouillon cultures beneath the mucous membrane. However, I succeeded in producing a small ulceration near the meatus on the penis of a rabbit. I had first injured the inside of the rabbit's foreskin by applying a hot piece of platinum foil and then applied several loops of culture. No growth took place at the site of the burn and the ulcer developed upon the opposite side of the glans.

The organisms in this ulcer were nearly entirely bacillary, but an occasional spirillum could be seen.

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**The Problem of the Amebic Dysentery Carrier in India and Mesopotamia.**—MACADAM and KEELAN (*Indian Jour. Med. Research*, July, 1917) discovered *Entameba histolytica* in apparently normal stools of numerous cases in the surgical division of the hospital, as well as in the medical wards, other than those assigned to dysentery. A systematic examination was then commenced and the present report is based upon the protozoölogical investigation of over 2000 men, mostly of the Mesopotamian field force, whose condition ranged from general good health to one associated with acute and chronic intestinal disturbances. Their records show that *histolytica* infection is so frequent that efforts at prophylaxis should be directed entirely to the purely sanitary aspect of the question. They believe that the segregation of any but the "gross" human carriers will remain an impossible and futile task until our therapeutic methods or the destruction of the cysts are more certain and effective. The results of treatment make doubtful the utility of attempting to clear men of *histolytica* infection while living under war conditions, or even while they continue to live in the tropics. Thus in a series of patients who gave an average of five negative examinations in hospital, after a residence of one week in the Convalescent Dépôt, a single reëxamination of the feces revealed the persistence of the infective agents in one-half of the cases. This shows the futility of any scheme for the clearing of dysentery patients where the protozoölogical examinations are entirely confined to the period during which the patients are resident in hospital. Also since 17 per cent. of total number of *histolytica* carriers, which they detected, gave no past history of dysentery, or marked diarrhea, they question the military advisability of prolonged segregation of dysenteric convalescents, who are otherwise healthy. By comparison with the findings of Dobell (Medical Research Committee, Special Report Series No. 4, 1916) it is found that the incidence of protozoal infection is distinctly higher in the Mesopotamian troops examined while still in the tropics, than in those patients who have returned to a more temperate climate.

W. H. F. A.

**Diseases of the Suprarenals in Soldiers.**—RAMOUD and FRANÇOIS (*Bull. Soc. Méd. Hôp.*, Paris, October 12, 1917) encountered 26 cases of disease of the suprarenals in their sector since last May. This is a higher proportion than would be found in times of peace, and it is inferred that the lowered resistance of the suprarenal is to be associated with the increased demands upon it produced by the continued mental and physical tension resulting from the war. This tension affects also other organs but especially the suprarenals which respond rapidly to various nervous stimuli, and which exercise control over the tonicity of various systems. Other authors have reported on evidences of suprarenal insufficiency as seen in cases with asthenia and psychasthenia, low blood-pressure and tachycardia and various gastric disturbances. Certain infectious diseases show more distinctly than in times of peace the mark of hyposecretion of the suprarenals such as typhoid and the paratyphoid fevers, dysentery, malaria, diphtheria, scarlatina, and diverse septiciemias. Vaccinations against typhoid and paratyphoid fevers sometimes cause marked disturbances of the functional activity of the gland. It is probable also that the asthenia so pronounced in those who have been gassed originates in great part from the same cause. The authors think it is this overexhaustion of the gland which exposes it to tuberculous infection. In this series of twenty-six, the suprarenals were tuberculous in nearly all, but rarely did the patients have pulmonary tuberculosis. Only four survived. Two of these showed evidences of associated hyperactivity of the thyroid, and the authors believe that inasmuch as the thyroids can function vicariously for the suprarenals, this thyroid hypertrophy was the means of defence. This idea is elaborated in the same journal, November 29, 1917 (p. 1131), where the clinical history of one of these two patients is given in detail. The patient had been at the front for two years without wound or illness. Then he began to experience great fatigue, and in three months showed clearly all the characteristics of disease of the suprarenals. Three months later when being examined he was found also to have an hypertrophied thyroid and other signs of Basedow's disease. This was six months after the beginning of the adrenal disease, and at this time, according to the declaration of the patient the feeling of fatigue began to diminish and the cutaneous pigmentation seemed to decrease. At any rate it is certain that during the two months he was under constant observation the skin did not continue to pigment, and in general the patient looked as if he were only at the beginning of suprarenal disease, not in the fifteenth month of it. The authors deduce that suprarenal disease complicated with Basedow's disease is relatively less serious than that of suprarenal disease alone. They also found that combined suprarenal thyroid opotherapy is the medication of choice in Addison's disease, but that even with this treatment, the results were markedly favorable in only three out of twenty-two cases.

W. H. F. A.

**Eye Changes in Trench Nephritis.**—KIRK (*British Med. Jour.*, January 5, 1918) examined a series of between 70 and 80 cases which had come to Malta from the Macedonian front. They were chiefly young men, and on arrival nearly all were seriously ill. At that time the fundi of a number of the patients were examined, and almost invariably

there was found marked retinal congestion with large pulsating veins. Some weeks later several complained of eye symptoms, and these on examination showed definite swelling of the optic disk with patches of retinal exudation. The whole series was then examined carefully, which was about three months after the onset of the illness. In those patients who were still severely ill, showing often a large quantity of albumin in the urine and sometimes blood, definite retinal changes were more distinct than in the patients who were convalescent. In these severe cases the spots of exudation were seen in the usual situations, near the disk and in the macular area. As the nephritic condition improved the smaller patches of exudation were gradually absorbed. Hemorrhages were not common, and those seen were of the small punctate variety, and not of the striate or flame-like character. The optic disk was often affected, the changes varying from a definite swelling to slight woolliness and indistinct edges. Small areas of edema were noticed especially along the course of the veins. The author suggests that the pathology is probably an acute congestion resulting from some specific toxin, that the exudation which ensues is partly lymphatic and partly cellular in nature, and that this deposit probably clears up in the great majority of cases, without leaving any permanent result. So the condition is one which is probably allied to the acute retinitis of pregnancy, scarlatina and acute uremia, and not to be confounded with the retinitis of chronic kidney inflammation with the accompanying permanent changes in the retinal circulation vessels and tissues.

W. H. F. A.

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**The Tuberculous Army Recruit.**—GAFFIKIN (*British Jour. of Tuberculosis*, January, 1918), while serving at a rest station behind the lines, made careful chest examinations of a large number of cases sent back for various minor ailments. During a period of four months he found the complete clinical picture of pulmonary tuberculosis in 1.9 per cent. Of these cases only a small fraction, about one-fifteenth, gave a history of previous tubercular disease. The conclusion is drawn that, as all these had been picked men, passed as fit for general service, a large proportion must have developed clinically observable phthisis during their service. This directly contradicts those who assert that the outdoor life of the soldier, the abundance and excellence of army rations, the regular hours and discipline of army life might be regarded as providing an excellent set of conditions for the recruit who shows signs of pulmonary tuberculosis either latent or arrested. The factor which outweighs all these is, according to the writer, the absence of rest. There is no rest in the trenches, and even when the unit leaves the trenches there is no adequate rest. Hence the French plan is commended, that a definite history of tuberculosis, with the exception of tuberculous lymphadenitis, should be regarded as a bar to enlistment for active service.

W. H. F. A.

## REVIEWS

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### THE SPLEEN AND ANEMIA: EXPERIMENTAL AND CLINICAL STUDIES.

By RICHARD MILLS PEARCE, M.D., Sc.D., EDWARD B. KRUMBHAAR, M.D., Ph.D., and CHARLES HARRISON FRAZIER, M.D., Sc.D. Pp. 419; 16 illustrations. Philadelphia and London: J. B. Lippincott Company, 1918.

THIS volume, presenting both the experimental and clinical evidences of the relationship of the spleen to anemia, reflects accurately the present state of our knowledge of this involved problem. The material is presented in three different sections by the respective authors, and covers the experimental, clinical and surgical phases of the subject.

The first section, by Dr. Pearce, presents the experimental groundwork on which is based our present ideas of the relationship of the spleen to blood destruction and regeneration. This section embodies the detailed studies which have appeared from the Department of Research Medicine of the University of Pennsylvania during the past few years. The various theories of the relationship of the spleen to the hemopoietic system are considered. Theories rendered untenable in the light of experimental evidence are discarded and theories supported by like evidence are emphasized. The effect of experimental splenectomy on the blood picture, the hemopoietic system, and metabolism is considered in detail. Numerous control experiments are reported and the evidence carefully sifted. Nowhere are sweeping conclusions drawn. On the other hand, the author endeavors to present a careful and concise summary of the present state of knowledge on the relationship of the spleen to the problems of blood destruction and regeneration, and in this the book is notably successful.

The second section, by Dr. Krumbhaar, presents the modern views on the classification, symptomatology, pathology and therapeutics of the various non-infectious splenomegalies. Of special interest is the chapter on the effects of splenectomy in pernicious anemia. The literature on this subject has been carefully reviewed and analyzed, and the conclusions drawn from this study are both interesting and valuable.

The third section, by Dr. Frazier, deals exclusively with the surgical aspect of the problem. The modern technic of splenectomy,

which has developed as the result of the more extended use of the operation in recent years, is given in detail.

The volume as a whole should fill a long-felt need, presenting as it does all our modern knowledge of the experimental, clinical and surgical phases of this many-sided problem. The entire literature of the subject is reviewed and an exhaustive bibliography attached. The volume is ably and adequately illustrated; the plates, many in colors, of the pathological lesions in the various splenomegalies being especially excellent. To the clinician this volume should be of great value for the intelligent study and treatment of the so-called "splenic anemias."

A. C. W.

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IMPOTENCE AND STERILITY, WITH ABERRATIONS OF THE SEXUAL FUNCTION AND SEX-GLAND IMPLANTATION. By G. FRANK LYDSTON, M.D., D.C.L., Formerly Professor of Surgical Diseases of the Genito-urinary Organs and Syphilology in the Medical Department of the State University of Illinois. Pp. 322; 26 illustrations. Chicago: Riverton Press, 1917.

UNTIL comparatively recent years little attention was paid to the subject of aberrations of the sexual function by the reputable physician, indeed the apathy exhibited toward diseases of this type usually encouraged the sufferer to visit the quack, who accordingly became fat and prosperous. In presenting this monograph on impotence and sterility, the author has covered the subject not only from the theoretical stand-point but has gone into quite some detail concerning the experimental work that has been done by himself and others and the practical application of such work. That he is a firm believer in the practicability of sex-gland implantation is evidenced by the fact that he transplanted a testicle from a dead body into himself with results that were quite satisfactory. To the reader, the account of this experiment together with the several other interesting and successful transplants would seem to indicate that Lydston had discovered the fountain of perennial youth which Ponce de Leon failed to find.

Granting that the author is correct in his belief that the results of his experiments have conclusively proved that transplantation of sex glands even from the dead body is both practicable and successful, the reviewer is willing to be considered somewhat conservative in hesitating to accept the proposition of advising transplantation in the treatment of senile dementia, dementia precox, neurasthenia, arteriosclerosis, psoriasis, various sexual perversions and the many other widely divergent conditions as suggested by the author, who is undoubtedly carried a bit too far by the enthusiasm resulting from a few of his experiments.

F. B. B.

TALKS ON OBSTETRICS. By RAE THORNTON LAVAKE, M.D., Instructor in Obstetrics and Gynecology, University of Minnesota. Pp. 151. St. Louis, Mo.: C. V. Mosby Company, 1917.

THIS little volume is presented by the author with the idea that it may supplement the text-book rather than supplant it and to this end it is written in a very interesting narrative style in the form of talks which the author has given to his students while waiting on labor cases in the out-patient department. In opposition to the usual theoretical considerations with which the average book is replete, this brochure is purely practical and presents to the student or practitioner the methods of prevention and treatment of the various obstetric complications in a manner which admits of no misunderstanding. Most of the statements are based upon the author's personal experience and are rationally conservative. Throughout the book there are two points which are continually emphasized and which prove that the author is presenting the latest knowledge on the subject; the first point is the plea of the author for the substitution of rectal for vaginal examinations in all but exceptional cases with the idea of reducing puerperal sepsis to a minimum and the second outstanding point of the book is the great stress which the author lays upon the importance of proper dental care for the parturient woman, thus reducing the various complications, perhaps including eclampsia, which result from such focal infections. On account of the numerous practical points which the book contains together with their ready accessibility, it would be an excellent idea for the student on out-patient labor cases to carry such a book in his obstetric bag. F. B. B.

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KIRKES' HANDBOOK OF PHYSIOLOGY. Revised and Rewritten. By C. W. GREENE, Professor of Physiology and Pharmacology, University of Missouri. Ninth American revision. Pp. 790; 509 illustrations. New York: William Wood & Co., 1917.

SEVENTY years of service must surely constitute a record in text-books, and it is now that period of time since Kirkes' *Physiology* first appeared. This was in 1848, just twelve years after William Sharpey, often referred to as the father of English physiology, became the first professor of physiology at University College, London, and gave there the first separate course of instruction devoted to this subject. Indeed, it might be said, that the history of this book in its various editions covers nearly the same period as that of the subject of physiology itself since its separation from anatomy. The work was originally written by William S. Kirkes, assisted by James Paget, both of St. Bartholomew's Hospital,

London. The first American edition appeared in 1849 and was published by Lea & Blanchard. Later on, in 1873, there appeared another first American edition from the eighth English, and dating from this the present volume is marked as the ninth American revision. By reason of these constant revisions the book still serves as a reliable source of present-day information for students of this branch of the medical sciences. In the present edition Professor Greene has made changes in the chapter on nutrition to call attention to the subjects of food factors necessary for growth and of vitamins and nutritional diseases, but otherwise the present volume differs but little from the preceding, and may be regarded as giving a conservative presentation of the subject.

W. H. F. A.

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DISEASES OF THE SKIN. By M. B. HARTZELL, A.M., M.D., LL.D., Professor of Dermatology at the University of Pennsylvania. Pp. 753; 242 illustrations, 40 colored plates. J. B. Lippincott Company, 1917.

THIS is an extremely good book! The author has availed himself of a very large personal clinical experience in the production of this work and has given a most creditable account of his observations, and the deductions he has made from these observations. He has expressed himself in his characteristic, fearless manner and has assumed responsibility for most of the views as to etiology, pathology, and treatment of the countless diseases described in the book. Comment must be made upon the illustrations, but only in praise of their originality and accuracy in depicting the features of the diseases under discussion. The photomicrographs are especially good and understandable. The text is unusually lucid and clear for a work on this subject. The sections upon diagnosis are especially readable. Treatment is dilated upon at great length. Unfortunately there are a number of remedies recommended, the names of which do not appear in the Pharmacopœia. Doubtless these are among the "New and Unofficial Remedies," but the average reader may not know that and the suspicion may arise in his mind, after a difficult, perhaps fruitless, search for the preparation, that the work is subsidized. An appendix containing notes regarding these preparations would not be inadvisable. As in any first edition of a book of this character there are a number of minor errors of interest only to the author and publisher which will be corrected immediately, but even these in the aggregate do not detract one iota from the value of this work. The author is to be congratulated upon this production. The reviewer has no hesitancy in placing this book among the foremost books on the subject in the English language.

S. H. B.

PRACTICAL MASSAGE AND CORRECTIVE EXERCISES. By HARTVIG NISSEN, President of Posse Normal School of Gymnastics; Superintendent of Hospital Clinics in Massage and Medical Gymnastics; Formerly Lecturer and Instructor of Massage and Swedish Gymnastics at Harvard University Summer School; late Director of Physical Training at Boston and Brookline Public Schools; Former Instructor of Physical Training at Johns Hopkins University and Wellesley College, Former Director of the Swedish Health Institute, Washington, D. C.; author of Swedish Movements and Massage Treatment. Pp. 211; 68 illustrations. Philadelphia: F. A. Davis Company.

THE first chapter of this book is devoted to indications for massage, the second to eleventh inclusive explain and discuss massage and manipulation in an elementary fashion, and very briefly. The twelfth to fourteenth inclusive take up in a most elementary fashion corrective exercises. From the fifteenth to the final chapter various conditions are discussed and their treatment by massage delineated. The author enumerates the following conditions: stiffness of the joints and tendons, morbid condition of the foot in which the arch is destroyed, hysteria and hypochondria, chlorosis and anemia, insomnia, diabetes mellitus, diseases of the brain, spinal cord and nerve, anemia of the brain, locomotor ataxia, infantile paralysis, occupation neuroses, cramp of various type, chorea, sciatica, circulatory, respiratory, genito-urinary, digestive diseases, appendicitis, scoliosis, rheumatism in various localities, specifically of the joints.

Many of the ailments noted would be benefited naturally by massage, but the fact that cure or correction of many of the maladies enumerated is intimated or claimed shows (1) the lack of knowledge of the etiology and pathology of these conditions, and (2) the methods of therapeutics which must be employed in rational treatment.

The order of the book is faulty, and as a hand-book is not well arranged in ready-reference fashion. As a text-book it is too brief and elementary to be of service to the advanced student of the subject.

W. J. M.

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LIGATIONS AND AMPUTATIONS. By A. BROCA. Translated by ERNEST WARD, F.R.C.S. Pp. 285; 510 illustrations. New York: William Wood & Co., 1917.

THE translator tells us that he has "simply translated the book as it is written, without editing or foot notes." Broca, himself disclaims any originality and says frankly that he has drawn his material entirely from Faraboeuf, claiming that the student hardly reads the work of the latter because it is too long and the operative



procedures described are too numerous. Broca describes only one procedure for each operation, and has prepared this digest only for students who take the knife in hand for the first time. The translator remarks that little alteration has been made in these branches of surgery in the last fifty years. The illustrations are original, diagrammatic and excellent.

T. T. T.

THE SURGICAL CLINICS OF CHICAGO FOR AUGUST, 1917. Pp. 207; 71 illustrations. October, 1917. Pp. 215; 84 illustrations. Philadelphia: W. B. Saunders Company, 1917.

THE high reputation of this publication, attained for it by Dr. John B. Murphy, is being maintained by the new plan of providing contributions from various noted surgeons, fifteen in the August number and sixteen in the October number. The style of presentation of the subjects varies from the brief case report to the more systematic treatment of the condition involved. Lucidity and compactness prevail and a large number of interesting conditions are discussed in a most practical manner. Because of the large number and wide variety it is difficult to particularize. Ochsner on Jacksonian epilepsy, Eisendrath on common duct calculi, Bevan on tumors of the breast, and Ridlon on hip disease deserve special mention. Shambaugh's report of a case of Ludwig's angina treated expectantly with recovery is unfortunate, since the treatment receives the credit of a cure due to the spontaneous evacuation of the pus into the mouth. This, however, is only 1 of 5 cases reported by this writer and does not impair the value of the remaining large amount of good material.

T. T. T.

RADIUM THERAPY IN CANCER AT THE MEMORIAL HOSPITAL, New York (First Report, 1915-1916). By HENRY H. JANEWAY, M.D. With the Discussion of Treatment of Cancer of the Bladder and Prostate, by BENJAMIN S. BARRINGER, M.D., and an Introduction upon the Physics of Radium, by GIOACCHINO FAILLA, E.E., A.M. Pp. 242; 18 illustrations. New York: Paul B. Hoeber, 1917.

THIS is a most valuable contribution on the subject of radium therapy, and is to be conscientiously recommended to all who are interested in radium as a therapeutic agent. The authors deserve the greatest praise for presenting a report of cases in a manner that attracts the interest of the reader and gives valuable assistance not only to those taking up the work of radium therapy but also to those

who have attained skill and experience. It is beyond doubt one of the most valuable contributions on the subject published in this country. In the introductory section Mr. Failla discusses, in a concise manner, the physics of radium, with special reference to a clear understanding of its application in treatment. This section of the book is particularly free from the rather abstruse technicalities with which the physicist is pleased to deal, but which appears so often as mere words or symbols, with little meaning to the physician. In the second section Dr. Janeway discusses the methods of application to cancerous and other lesions. After a general consideration of methods and applicators a general report is made of each class of cases, with detailed case reports of representative cases. These reports are especially valuable because of the careful attention given to the description of the technic employed. The third section comprises a summary of 55 cases of carcinoma of the bladder and prostate treated by radium.

H. K. P.

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ON THE ALLEGED INCREASE OF CANCER. By WALTER FRANCIS WILLCOX. Reprinted from the Journal of Cancer Research, July, 1917, Vol. II, No. 3. Pp. 98.

THE author concludes that it is "probable, although far from certain, that cancer mortality is not increasing." The alleged increases are due (1) in greatest part to increased reports of inaccessible cancer (abdominal, etc.), due to improvement in diagnosis, and (2) changes in age composition of population. F. D. W.

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PHYSIOLOGICAL MEDICINE. A MANUAL ON MENTAL DISEASES FOR PRACTITIONERS AND STUDENTS. By MAURICE CRAIG. Third edition. Pp. 484. Philadelphia: P. Blakiston's Son & Co., 1917.

THIS is the third edition of this excellent manual on mental diseases. In this book of less than 500 pages the subject of mental medicine is discussed very well, and altogether it is one of the best of the shorter expositions of psychiatry. It takes the older view-point of mental diseases. Besides it has 27 plates, which show the different alterations of the nervous system present in different types of mental diseases. These plates are excellent.

This book contains a new chapter on the psychoneuroses occurring in the men exposed to shell shock and strain in war. The author makes the interesting statement: "Already French observers have reported that shell-shock cases examined in field hospitals within a

very short time of the concussion exhibit symptoms which in the patient have been regarded as pathognomonic of organic disease. Such symptoms are the plantar extensor reflexes, absent knee-jerk, and absent cutaneous reflexes, etc. So far as the mental conditions arising from war are concerned, the author states that there has not been any development of any special war type. T. H. W.

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AN INTRODUCTION TO THEORETICAL AND APPLIED COLLOID CHEMISTRY. By DR. WOLFGANG OSTWALD, Privatdozent in the University of Leipzig. Authorized translation from the German. By DR. MARTIN H. FISCHER, Eichberg Professor of Physiology in the University of Cincinnati. First edition. Pp. 232; 45 illustrations. New York: John Wiley & Sons, Inc., 1917.

THIS book consists of five lectures, the material for which was gleaned from a series of lectures given by the author in many of the universities in this country. The attempt is made, and successfully so, to give a general survey of modern colloid chemistry as a pure and as an applied science. Furthermore, the subject is treated in a way that makes it intelligible to the general reader.

The author believes that with radiochemistry was born a twin science, the fruits of which are no less wonderful and the application possibilities of which to all branches of science, to technology, and to industry are not only equal to but exceed those of radiochemistry. Certain it is that the importance of colloid chemistry is coming to be appreciated more and more, and this volume, the author designates a propaganda sheet for colloid chemistry.

The first three lectures deal with the fundamental properties of the colloid state, colloids as examples of dispersed systems, methods of preparing colloid solutions, classification of the colloids, physico-chemical properties of the colloids and their dependence upon the degree of dispersion, and the changes in state of colloids. The fourth lecture treats of some scientific applications of colloid chemistry, and the fifth lecture deals with some technical applications of colloid chemistry.

The book is well written, easily read and mechanically leaves little to be desired.

The author might have done well to omit entirely the addendum to the preface, or at least to omit that part of the addendum in which reference is made to the "justice of my Fatherland and of its power to carry matters to a victorious conclusion."

H. D.

# PROGRESS OF MEDICAL SCIENCE

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## SURGERY

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UNDER THE CHARGE OF

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**An Anatomical Point which Facilitates the Location and Delivery of the Appendix.**—GUTHRIE (*Ann. Surg.*, 1917, lxy, 742) says that the method described can only be employed in cases in which the appendix lies free in the abdomen. Through a muscle splitting, or McBurney's incision, the index and middle fingers of the left hand are inserted into the iliac fossa. The cecum, lying directly underneath, is lifted well up in the iliac fossa by a cat's-pawing action of the fingers until the head is located. The fingers are then swept along the course of the iliac vessels from without inward, describing the arc of one-fourth of a circle, until the point of attachment of the root of the mesentery is reached. This is felt as a band, which marks the location of the ileocecal juncture. The base of the appendix, if lying free in the abdomen, should be within three-fourths of an inch from this point. If the hand is now elevated slightly anteriorly and the fingers moved about, the appendix, as a rule, can be found. Grasped between the fingers it can be delivered from the wound. Should a right rectus or midline incision be used the band is located by sweeping the fingers in the opposite direction, *i. e.*, from within, outward, and upward.

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**Observations in Military Surgery** —CLARK (*Surg., Gynec. and Obst.*, 1917, xxv, 463) says that in spite of the steel helmets, wounds of the skull are frequent. The surgeon is between the two evils of immediate meningitis if he closes the wound and cerebral hernia if he leaves it open. In the great majority of cases conservative surgery has no place in the military practice of the present war. Foreign bodies are being removed as a routine by aid of new instruments of localization. There is a tendency to remove all loose bone fragments in shattered fractures but the method lacks the support of statistics of ultimate results. Important factors in the reduction of mortality are Carrel technic in wound infections, guillotine or *coup de hache* method of amputation, routine use of antitetanic serum, oxygen injections for gas-bacillus infections. Very early in the war it was found that the shaping of the

classical flap in doing a primary amputation was a waste of time and tissue. The infection which followed invariably resulted in sloughing of the flaps which demanded a secondary operation, and in some cases a reamputation. It was found expedient to perform a rapid amputation of all tissues, skin, muscle, and bone, at the same level, what the French call *coup de hache*. Aside from ligature of vessels, nothing is done but the straight cut across, severing the part as it might be done by laying it on a block and clipping it off with a headsman's axe. In the wide-open wound thus formed the infection can be easily controlled, and cleared up. In the meantime the soft parts have a tendency to contract away from the bone, and in the thigh cases this is sometimes serious, as the surgeon seeks to conserve as much tissue as possible. To overcome this contraction it is necessary to apply wide adhesive straps at four points around the stump and attach a weight of from five to ten pounds, which will hang over a pulley at the foot of the bed and maintain a constant traction against this retraction of the skin and muscle. When the granulations begin to form and the pus is all gone the plastic repair of the stump is done, including reamputation of the bone and of the nerves and the shaping and suture of the flaps.

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**Fascia Transplantation into Visceral Clefts.**—NEUHOF (*Surg., Gynec. and Obst.*, 1917, xxiv, 383), after a study of the literature and a series of experiments on dogs, says that the free transplantation of fascia into aseptic fields has a wide sphere of usefulness. It has proved very satisfactory in the replacement of thoracic defects, of aponeurotic defects in operations for various types of hernia and of defects of the cranial dura. Fascia transplants have been very successfully used, in a variety of ways, for the reinforcement or replacement of ligaments, tendons, and paralyzed muscles. They have proved effective as coverings for wounds of solid organs, especially the liver. Their usefulness has not been clearly demonstrated in other aseptic fields; as shields for the isolation of nerves, as strips for occlusion of the pylorus, in fixation or suspension of organs, for separation of joint surfaces. There are many advantages of fascia over other tissue transplants (fats, muscle, periosteum, etc.), for the purposes mentioned. Fascia (lata) is most readily accessible and is obtainable in almost unlimited quantities; its removal does no damage. Transplanted fascia has a remarkable tendency to heal in place even under most disadvantageous conditions, requiring minimal nourishment to obviate necrosis. It combines great tensile strength, with slight tendency to stretch or contract. It is most readily adaptable to the shape of any organ, and, technically, can be most easily handled. Finally, fascia can be transplanted autoplastically. The ultimate fate of transplanted fascia has not been definitely determined. Of practical importance is the fact that the resultant firm, connective tissue is as serviceable as the original transplant. Experimentally, fascia transplants have been found satisfactory for the reinforcement of suture lines in hollow viscera. They were successfully employed in a few instances to bridge small tracheal fistulae, and they occasionally prevented leakage from small esophageal and bladder fistulae. These occasional satisfactory results were found to depend upon healing by contraction of the defect. For this reason failure followed every experimental effort to replace appreciable esophageal and vesical defects. The technic employed in these

experiments on hollow viscera (and on other organs) was the attachment of the transplant over the defect. To offer any chances for uniform success a method evidently was required to prevent the cut margins of the organ from rolling back, to give sutures a firmer hold on the organ by passing them through all its layers, to more readily supply the graft with provisional nourishment, and to invite the overgrowth of the lining mucous membrane of the organ. It is demonstrated in this paper that these requirements were met satisfactorily by suturing fascial sheets into instead of over defects of hollow viscera (and of other organs).

**The Value of the Leukocyte Count in the Diagnosis and Prognosis of Acute Appendicitis, as Based on Experience in One Hundred Cases.**—HEWITT (*Ann. Surg.*, 1917, lxvi, 143) says that the counts here submitted have all been taken from cases of appendicitis clinically acute, and in so far as he has been able to ascertain no coexistent infection has been present. All counts were taken within a few hours of operation and the great majority were taken immediately before the administration of the anesthetic. The wide variation noticeable in the counts reveals the widely variant acuteness of the infection and the effort exerted by the resisting forces of the body. The absolute count when taken alone is of questionable value. The polynuclear count alone is, in the great majority of instances, a reliable index in diagnosis. The correlated absolute and polynuclear counts are of greater value than either count taken alone, especially as regards prognosis. A high absolute count with a high polynuclear count means usually a good prognosis (*e. g.*, absolute 35,000, polynuclear 95 per cent.). A high absolute count with a moderately low polynuclear (*e. g.*, absolute 30,000, polynuclear 80 per cent.) means usually a very good prognosis. A low absolute count with a high polynuclear count (*e. g.*, absolute 7000 with polynuclear 95 per cent.) indicates a grave prognosis (speaking generally). A low absolute count with a low polynuclear count (*e. g.*, absolute 7000 with polynuclear 65 per cent.) usually means no infection, or that the acute condition is due to anatomical or mechanical causes; in other words, that the infection, if one be present, has not stimulated the resisting powers of the body sufficiently to produce a leukocytosis. Normal or subnormal figures do not necessarily indicate the absence of suppuration, gangrene, or their sequels. Catarrhal cases, fulminating cases, moribund cases, and walled-off abscesses frequently do not stimulate leukocytosis.

**Retention of Ovarian Tissue after Hysterectomy.**—GRAVES (*Surg., Gynec. and Obst.*, 1917, xxv, 315) says that specific surgical menopause symptoms consist chiefly of vasomotor disturbances in the form of hot flushes. Theoretically, vasomotor changes of the artificial menopause are due to a break in the uteroövarian functional harmony by which the physiological balance of the glands of internal secretion is upset with consequent disfunctional activity. After extirpation of the uterus, vasomotor disturbances ensue, with approximately equal frequency, whether the ovaries be retained *in situ*, totally ablated, or transplanted. Retention of ovarian tissue after hysterectomy is of little or no physiological value, and may be of serious harm to the patient.

## OBSTETRICS

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.,

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**Puerperal Septicemia Treated by Autogenous Vaccine, with Recovery.**—GRIER (*British Med. Jour.*, September 30, 1916) reports the case of a woman who had a twin labor, the first child delivered in breech presentation and the second in vertex. There was a slight tear of the perineum. The patient continued well until the afternoon of the eighth day, when she felt hot and flushed. On the following morning she complained of pain behind the left shoulder. She became nauseated and vomited freely. The temperature was  $101^{\circ}$  F., and the pulse 100. The lochia was not foul and there was an abdominal tenderness. The secretion of milk was abundant. She had superficial inflammation of the gums associated with carious teeth. The patient complained of rheumatic pain in the left shoulder and over the left elbow. On the seventh day the temperature rose to  $104^{\circ}$  F., pulse 120 to 130, the secretion of milk had ceased, and there was severe pain and tenderness. The temperature continued high, and the patient had severe chills chiefly at night. She complained of pain in the right groin. The inguinal glands were swollen, enlarged, and were associated with a pustular eruption on the pubis. On the ninth and eleventh days of her illness she was given 20 to 25 c.c. of antistreptococcic serum, and on the thirteenth day 25,000,000 streptococcic vaccine, made from a fatal case of puerperal septicemia, were injected. An autogenous vaccine from the patient's own blood was prepared, the culture being a pure growth of a short-chained diplostreptococcus. Of this, 25,000,000 organisms were injected on the sixteenth day of her illness, and on the eighteenth day 50,000,000. Every third day after this she was given 50,000,000 until near the end of her illness, when she had 75,000,000. She had a well-marked, fine, discrete, papular rash resembling scarlatina, appearing first on the face, neck, chest, and upper extremities, and on the following day on the lower portion of the body. The eruption did not itch and desquamation occurred after the eruption had disappeared. This was followed by a fall in temperature, and then a rise from a pus formation over the right shoulder. After this had been opened the temperature gradually fell to normal. The writer is inclined to believe that the case was one of scarlet fever developing during the puerperal period.

**Puerperal Gangrene of the Extremities.**—STEIN (*Surg., Gynec. and Obst.*, October, 1916) reports 2 cases of puerperal gangrene of the extremities. The first was a young, vigorous primipara who, shortly after admission to the hospital, aborted at three months. There was a foul odor from the fetus as well as from the vagina. Following this there was some rise in temperature, which dropped again to normal. This was followed by another rise to  $104^{\circ}$  and  $105^{\circ}$  F., for the next six days, with no pain and no other symptoms. On the seventh day it

was decided to curette the uterus, and on examination there were numerous grayish-white, superficial ulcers around the cervix, covered with whitish membrane. The curette brought away a small portion of placental tissue. After curetting the interior of the uterus and cervix were thoroughly swabbed with tincture of iodine. This was repeated for the next seven days. Seven days after the curetting the patient complained of pain in her right leg, and ten days after curetting the right leg and foot began to swell, became cold, and showed violet-bluish discolorations. The pulsation of the dorsalis pedis artery was not felt and the foot was very painful. Deep sensation gradually disappeared. The Wassermann test was negative. The whole foot ultimately became gangrenous, the swelling extended  $2\frac{1}{2}$  to 3 inches above the ankle, where a line of demarcation could be seen. Amputation had finally to be performed below the knee. The patient made a good recovery and left the hospital in good condition. The heart had always been normal and several blood cultures showed no growth, especially no hemolytic streptococcus were found. On microscopic examination the characteristic lesions of gangrene were present, with thrombosis of the peroneal artery, venous thrombosis, and necrosis of the skin, fascia and muscle. His second case was a forceps delivery at full term in a primipara who was in good condition and in whom the Wassermann examination was negative. She was delivered with medium application of forceps, and a second degree laceration was repaired with chromic catgut suture. Two days after confinement the patient had a temperature of  $104.5^{\circ}$  F., and a chill. Slight ulcers were found about the cervix, which were treated by iodine applications and douches. The urine showed a trace of albumin and hyaline casts. On the sixth day after confinement the sutures in the perineum were removed because the whole area was sloughing. Ten days after labor the patient had an irregular temperature, rising to  $103^{\circ}$  and  $104^{\circ}$  F., and, on the eleventh day, to  $105^{\circ}$  F. On the twelfth day after confinement the patient left the hospital against the advice of the physician, but returned seven days later in a critical condition. Both feet for about four inches above the ankle were discolored, nearly black, and the skin shrivelled. The feet were extremely tender when touched, cold, and in some places showed vesicles filled with whitish fluid. The line of demarcation was well pronounced about four inches above the ankles. There was no pulsation in the femoral arteries. The patient died about one month after delivery from extreme exhaustion and debility. Several cultures made from the blood showed there was general septicemic infection. An autopsy could not be obtained. The writer has collected 76 cases, whose reports seem authentic, of which 63 were cases of puerperal gangrene following labor with one personal observation, the author's second case; and 4 cases after abortion with a personal observation, the author's first case; 4 cases occurred in the late course of pregnancy and 5 cases after gynecological operations, which had been added for reasons of completeness. These cases are gangrene, due to the puerperal state and affecting the extremities. This condition may arise from puerperal thrombosis or embolism, which occurs in 1 in 500 births and 1 embolism in 9000 births. A considerable loss of blood predisposes to this condition, and so does an abnormal constitution of the blood. Although the veins of the genital apparatus are often diseased during pregnancy, peripheral puerperal gangrene of



venous origin is very rare. Although phlegmasia alba dolens is not uncommon, it rarely, if ever, terminates in gangrene. The arterial origin of peripheral puerperal gangrene is far more common and is probably always due to infection. The rise of temperature commonly seen in thrombosis after childbirth is undoubtedly due to infection. One can readily understand how such thrombosis can occur should the blood become infected through bacteria lodged at the placental site. The development of gangrene will depend largely upon the question as to whether the collateral circulation after thrombosis can be maintained. When both veins and arteries are blocked the condition is that of arterio-venous puerperal gangrene. It may be difficult, if not impossible, to decide that a given case is of this variety, because it is impossible to differentiate between primary and secondary thrombi. The most usual cause of this condition is puerperal pyemia resulting in septic endocarditis, with involvement of the valves of the heart from which infected emboli are carried into the circulation. The mechanical conditions after childbirth are all favorable to the development of such complications. The symptoms of incipient gangrene naturally vary with the origin and path of the infection. Pain is severe and never absent in extensive vascular obliteration, such as lead to peripheral gangrene. The ordinary symptoms of puerperal fever usually develop, but there are signs of tissue necrosis. Septic puerperal endocarditis, as a rule, is present. Sometimes the gangrenous symptoms will suggest the cause and seat of the obstruction in the circulation. When the attack begins suddenly the indications are that embolism in the arterial system has developed, but when gangrene makes itself known very gradually the obstruction is in the venous circulation. In a general way it may be said that the early appearance of gangrene in the first few days after childbirth indicates its arterial origin. The manifestations usually seen in gangrene are severe pain, absence of arterial pulsation below the thrombus or embolus, and sensibility is diminished while motility may be preserved. A livid discoloration and relatively diminished temperature in the affected area indicate incipient gangrene. In cases of venous origin it may be possible by examination through the vagina or rectum to palpate the inflamed veins in the broad ligament. Sometimes dry and moist gangrene are combined in the same case, depending upon the rapidity of the complete interruption of the blood current and the presence of external factors which favor mummification. The pain is usually better when gangrene has become established, but the patient's general health suffers. Death may occur before demarcation is established, with increased pulse and temperature. The prognosis depends upon the patient's condition. If she is sufficiently strong to bear amputation her chance for recovery is greatly improved. It is not always practicable, because of the patient's bad condition or the rapid progress of the gangrene, or because the seat of the obstruction is located high up in the aorta. From one-half to two-thirds of these patients die. The mortality has been lessened about half by modern methods of treatment. The treatment consists in purely conservative measures, such as elevating the affected limb, giving stimulation to the heart, transfusion, and similar measures. The line of demarcation is the signal for surgical interference. Although the dangerous symptoms may apparently subside it is best to remove the gangrenous part as promptly

as possible. Prophylaxis consists in the best of hygienic, aseptic, and antiseptic management of deliveries, the improvement of the local circulatory conditions through elevation and gentle massage, and the aseptic and antiseptic management of lesions of the skin. The majority of the cases suffered from peripheral gangrene of the lower extremities. After abortion, gangrene of the lower extremities must be comparatively rare, as but 3 cases have been collected. Gangrene of the upper extremities in the puerperal period is also rare.

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## GYNECOLOGY

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UNDER THE CHARGE OF  
JOHN G. CLARK, M.D.,

PROFESSOR OF GYNECOLOGY IN THE UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA.

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**Bacteriological Study of the Endometrium.**—Some of the most interesting and at the same time most useful studies that have been elaborated by an American gynecologist in recent years have been those of Curtis, whose past work along the line of leucorrhea and other endometrial disturbances are probably familiar to all. It is fitting therefore to call attention to the latest presentation of this worker, which consists of a combined bacteriological and histological study of the endometrium in health and in disease (*Surg., Gynec. and Obst.*, 1918, xxvi, 178). The work is based on observations made upon a series of 118 cases. It was Curtis's object to make a study of the endometrium, exclusive of the cervix, in all conditions usually encountered except those associated with pregnancy. All of the material used was secured from uteri removed at operation. Scrapings from the endometrium are so liable to contamination that cultures from them are not included in this series. The technic that was employed in securing the material for this study consisted in cauterizing the stump of the cervix and the entire length of the peritoneal surface of the uterus and then bisecting the anterior wall. With sterile instruments the greater part of the endometrium is excised in its entire thickness down to the muscle layer, and is placed in sterile containers to be ground and cultured. The remainder serves for immediate examination and for microscopic study. The reason for undertaking such a study as this is because Curtis believes that it is especially desirable to compare histological evidences of chronic inflammation of the endometrium with cultures from the same material. Though we are interested in the frequency with which the endometrium yields histological signs of endometritis, after all a problem of more vital clinical importance is whether bacteria live in those tissues which are altered. We wish to learn whether the presence of mononuclear cells in a given piece of tissue means a possible focal infection of the uterus, and we need to know whether such a uterine cavity can be handled with impunity at operation or must be considered a zone of danger from which infection may spread. In the classification of cases studied it has

seemed best to distinguish between nulliparous and parous patients. Among the latter pregnancy has introduced the possibility of fundus contamination and has also rendered the cervical canal relatively more patent for the ascent of germs into the uterus. Each of these two groups has again been divided into those in which the history has been normal and those with history or operative evidence of pelvic infection. Group 1. The endometrium of nullipara without history of infection. Of 26 supposedly non-infected nulliparous cases, cultures and tissues were normal in 23. Streptococci were isolated from 1 case, while in 2 other cases, which had been eurented respectively eight and six days before hysterectomy, mixed growth appeared in the cultures and the histological evidences of endometritis were present. Group 2. The endometrium of nullipara with history of gross evidence of pelvic infection. Of the 13 patients in this class 12 yielded no growth. Histologically 9 of these were normal, 1 showed tuberculosis, 1 a slight cellular infiltration and 1 was invaded by polynuclear and plasma cells. The endometrium of a case with recurrent infection of sixteen years' duration yielded gonococci in cultures and histological evidence of chronic endometritis. Group 3. The endometrium of parous women without history or gross evidence of pelvic infection: Of the 47 women in this class, in only 2 cases did the endometrium show growth. One of these patients, with intra-uterine manipulation preliminary to operation, yielded a moderate number of colonies in mixed culture and was microscopically normal. The other, a victim of persistent uterine hemorrhage, showed anaërobic streptococcus infection and microscopic evidence of endometritis. Group 4. The endometrium of parous patients with history or gross evidence of pelvic infection. Of the 32 patients belonging in this class 9 showed a growth in the culture of the endometrium; 4 of these, regularly exposed to reinfection, yielded gonococci and showed histological subacute endometritis. Another without exposure for six months had inflammation of the endometrium and Fallopian tube with gonococci from both. Two cases of many years' standing yielded respectively a diplococcus and a streptococcus. Ten endometria without growth proved microscopically normal, 2 contained round cells, 1 a postmenstrual polynuclear increase, 7 had plasma and round cells and 3 revealed distinct histological endometritis. As a result of these extensive investigations, Curtis has come to the conclusion that, pyometra and recent exploration of the uterus excepted, the endometrium almost never shows bacteria except when there is infection of adjacent pelvic tissues. Chronic endometritis *per se* with bacteria present in smears or cultures is practically to be ruled out as a clinical entity. Several points of clinical importance come up in this work. In the first place we may consider infection of the endometrium consequent to curettage. In certain cases normal scrapings have been obtained from the uterus; then, several days thereafter, in the endometrium secured by hysterectomy mixed cultures and endometritis have been found. Infection is perhaps not a customary result of curettage, but it appears not uncommon. This calls attention to the fact that preparation for instrumentation of the uterine cavity does not ordinarily include cleansing of the cervical canal, yet this tissue is freely accessible to all vaginal flora. Curtis believes, therefore, that it is a wise precaution to gently introduce an iodine applicator as far into the cervix

as it is patulous before attempting to pass instruments. In regard to the problem of intra-uterine therapy, it has been found that chronic infection of the corpus uteri speaks for almost certain involvement of other pelvic organs. Intra-uterine applications are therefore of little avail, for the most important focus of infection is well beyond their reach. Again, in the absence of bacteria it may be desired to rid the patient of a persistent discharge. Study of this question makes it appear that mucus secreted from the body of the uterus is in very small amount and limited mostly to the premenstrual period. In the cervix are glands, prolific in activity, especially adapted to mucous secretion. It is here, in the cervix, up to the level of the internal os, that we will do best to look for infection, and it is against discharge from the cervix that treatment can be efficiently directed.

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## OPHTHALMOLOGY

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**Physiological Tension of the Eyeball.**—In an extensive study of this subject running through three numbers of the *Ann. d'Oculistique*, May, 1917, p. 272; June, p. 334; July, p. 385) MAGITOT sums up as follows: The normal tension of the eyeball oscillates between 15 and 25 mm. Hg.; it may vary between these limits from day to day and even during the same day. It is apparently lower in the aged than in the young. The tension corresponds to variations of the general arterial pressure, though the globe possesses an autoregulating mechanism which serves to oppose increase of pressure. The factors capable of influencing the ocular tension are: (a) the general circulation, (b) the local circulation, (c) the structure of the walls of the globe itself. The latter is extensible in the adult to a certain degree, owing to the numerous elastic fibers of the sclera. The variations of the tension within normal limits are due principally to the variations of the general arterial pressure, a relationship which may be compared to that of the pulse and the temperature. But the intra-ocular tension responds to a far greater degree to variations in the local circulation than to those of the general. Among nervous influences the cervical sympathetic or its ganglia is alone capable of influencing the tension of the globe, and not the trigeminal. Section of the cervical sympathetic or superior cervical ganglion produces slight *hypertonia*; excitation determines a *hypotonia* in all animals. The sympathetic centers capable of modifying the ocular tension are three in number: (a) the bulbomedullary

centers (primary centers) possess an action particularly dilating; (b) the cervical and cephalic centers (secondary centers) possess an action particularly constricting; the action of the ocular center (c), tertiary center, is variable. Of these centers the role of the ocular is the most important; it is the true regulating organ. The aqueous humor has no influence upon the ocular tension. Collyria have little influence. The slight effect which they exert depends upon their action upon the diameter of the uveal vessels. Finally, the tension of the globe is solely under the influence of the greater or less repletion of the ocular vessels. These vessels are themselves governed by the vasomotor nerves. But the capital importance which the sympathetic ocular center (tertiary center) plays in the innervation cannot be too much insisted upon.

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**Acute Infectious Retrobulbar Optic Neuritis.**—LENOIR (*Ann. d'Oculistique*, July, 1917, p. 411) argues that this condition possesses a special symptomatology which differentiates it sharply from other diseases of the optic tract. The functional disturbances consist of rapid and frequently great diminution of the visual acuity, with deep periorbital pains, increased by pressure upon the globe and extreme excursions of the same. The ophthalmoscopic appearances are ordinarily slight or absent, simply at times some infiltration of the optic disk. There is an absolute central scotoma, and more rarely, irregular contraction at the periphery. The affection develops rapidly in the course of a few weeks, and generally heals without notable visual impairment in spite of the atrophic appearance of the disk. Alternating, relapsing and binocular cases occur, but in the latter the two eyes are always affected successively and the evolution of the lesions presents no symmetrical character. The disease is frequently complicated by more or less severe disturbances of the nervous system, which may simulate intracranial hypertension, but of which the prognosis is favorable. The cause cannot be attributed to sclerosis *en plaques* nor to syphilitic or rheumatic infection, but presents all the marks of an infectious lesion. Frequently consecutive to mild infections of the rhinopharynx it seems in certain cases to be dependent upon lesions of the sinuses, particularly the sphenoidal. Whatever be the origin the inflammation of the sheath of the optic nerve causes compression of the nervous elements, of the macular bundle in particular and lesions of degeneration whose gravity is in direct ratio to the duration and intensity of the inflammatory process.

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**Ocular Signs of Death.**—TERSON (*Arch. d'Ophthal.*, May-June, 1917, p. 513) describes the early and late ocular signs of death. The reaction of the pupils was found to be variable. They responded slowly to light, as also to atropin and physostigmin for several hours after death; electricity sometimes contracted the pupil five or six hours after death. Cauterization, scraping, sulphate of copper and subconjunctival saline injections produced no redness in the still warm body two hours after supposed death. Instillations of ether may cause damage; the reporter prefers dionin, which is followed by no reaction if applied two hours after death. These reactions may lead to important results in early cases of apparent death when other signs are still wanting.

**Sympathetic Uveitis.**—MORAX (*Ann. d'Oculistique*, July, 1917, p. 426) shows that sympathetic infection may have, as its point of departure, traumatic lesions both of the anterior and posterior segments of the globe; the former are much the more common. Anatomopathological studies of the sympathizing eye present uniformity of choroidal lesions, characterized essentially by a nodular or diffuse thickening of the choroid from penetration of lymphocytes between the uveal layers. The writer holds that all microbiological researches (direct examination, cultures, inoculation) have given a negative result and that the idea of microbic infection must be abandoned in this disease. Anatomical researches have convinced him, as they have others, that the uveal inflammation shows identical lesions which constitute a characteristic picture. He believes that the introduction of a new technic or modification of those already known will hereafter disclose the active agent of this infection.

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**Ocular Affections in Pest.**—YUUDINE (*Więstnik Ophthal.*, t. xxvii, 21) has examined 19 eyes of 15 individuals dead of pest; 16 were enucleated two or three hours and 3 ten to thirteen hours after death. The lesions discovered were localized principally in the posterior segment, in the choroid. The author believes that iridocyclitis, serous iritis and non-suppurative kerato-iritis result from the propagation of the inflammatory process of the uveal tract. The lesions observed are as follows: The veins and capillaries of the choroid are widely dilated, especially marked in the posterior portions of the choroid near the optic disk; in the neighborhood of the ciliary body the dilatation is less. In some of the eyes the dilated vessel was seen in the section to fill up almost the entire thickness of the choroid. The vessel walls are thinned, the endothelium swollen. In some cases the wall was necrotic, the degenerated tissue being sometimes swollen and sometimes granular. In one case which lasted thirty-four days there was hyaline degeneration of the walls of the small vessels. The layers of the choroid contiguous to the retina were fitted with an exudate consisting of a structureless mass, filaments of fibrin, globules of hyaline and pigmented granulations; the same exudate also penetrated between the choroid and the retina. The latter membrane was thickened and its vessels gorged with blood; the vessel walls were distended with liquid, the perivascular spaces dilated. The nuclei of the endothelium were swollen at some points so as to project into the lumen of the vessel. The ganglion cells were slightly pigmented. The cells of the internal and external granular layers were swollen and showed a lack of chromatin. In the internal nuclear layer cystoid degeneration had taken place. In all the eyes examined the retina was more or less detached from the above-mentioned exudate between the choroid and retina. Bacteriological examination was negative in every case as regards the bacilli of bubonic plague. This negative result favors the opinion that the ocular lesions were due to toxins of the bacilli.

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**Ocular Manifestations of Icterohemorrhagic Spirochetosis.**—WEEKERS and FIRKET (*Arch. d'Ophthal.*, September-October, 1917, p. 647) show that this infection gives rise to frequent and diverse ocular manifestations; these are icterus of the conjunctiva, simple hyperemia

of the anterior segment of the eyeball, congestion of the iris, iritis, optic neuritis, retrobulbar neuritis, ocular herpes and subconjunctival hemorrhages. Hyperemia of the anterior segment, congestion of the iris and iritis are all probably phenomena due to a variable degree to a localization in the highly vascular uveal tract of the spirochete circulating in the blood just as it becomes fixed in the hepatic and renal tissue. These alterations in the uvea are generally benign; they may even recover spontaneously and easily yield to appropriate treatment. Optic neuritis and retrobulbar neuritis, likewise benign, are probably related to the presence of the spirochete in the cephalorachidian fluid and in the liquid which bathes the sheaths of the optic nerves. Ocular herpes is rare; it may give rise to lesions of the globe itself, particularly of the cornea, and thus cause permanent damage to the sight. Icterus of the conjunctiva and subconjunctival hemorrhage are of no special significance as regards the eye.

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## DERMATOLOGY

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UNDER THE CHARGE OF

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**Intravenous Foreign Protein in the Treatment of Psoriasis.**—SCULLY (*Jour. Am. Med. Assn.*, November 17, 1917) reports favorable results in psoriasis from the injection of a foreign protein, the protein employed being a typhoid vaccine containing 100,000,000 organisms to each cubic centimeter. From three to five injections were given at intervals of three or four days, and following the third injection a 2 per cent. chrysarobin ointment was used on the body and a 5 per cent. ammoniated mercury ointment on the scalp and face. His conclusions are as follows: Intravenous vaccines alone do not clear up the lesions of psoriasis, though they do lessen the induration and inflammatory reaction. When used in conjunction with chrysarobin ointment the lesions clear up rapidly. Favorable results were obtained in chronic generalized cases resistant to other forms of treatment. Chrysarobin dermatitis is prevented by the vaccine, and when present yields promptly. (We must confess to a very decided skepticism as to the real value of these injections; it is to be kept in mind that the eruption of psoriasis frequently diminishes or even disappears for a time without any treatment.—M. B. H.)

**Treatment of Frost-bite.**—CAMESCASSES (*Le Bull. Med.*, January 26, 1918) highly recommends the following mixture in the treatment of frost-bite: Picric acid, 0.25; alcohol, glycerin, aa 10. This is painted over the affected parts twice a day, allowed to dry and should not be wiped off. After the second application the itching, pain, redness and swelling disappear. When ulcers are present, these are treated with zinc oxide paste.

**Results Obtained by Heiser's Treatment of Leprosy in Nigeria.**—COGHILL (*Ann. Trop. Med. and Parasit.*, August 23, 1917) used the mixture recommended by Heiser, viz., 60 c.c. chaulmoogra oil, 60 c.c. camphorated oil and 4 grains of resorein. Of this mixture, which was sterilized by boiling, 2 c.c. were injected into the buttocks as an initial dose and the dose was increased 1 c.c. per week until 8 c.c. were being given at intervals of a week. As this dose, however, produced some discomfort it was reduced to 6 c.c. twice a week, which was well tolerated. Every case responded to the treatment. The most obvious effect was the healing of ulcers, many of which were extensive and had lasted for many years. Softening and absorption of the nodules, fading of macules and return of sensation were also noted, not only by the author but by the patients themselves. As this treatment was begun only in 1916, he believes it too early to decide whether it is actually curative.

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**Treatment of Scabies by Sulphur Fumigation.**—BRUCE (*British Jour. Dermat.*, April-June, 1917) finds fumigation with sulphur a rapid and certain method of treating this most annoying affection, which is extremely prevalent at this time in the armies of the Allies. The treatment is carried out in the following manner: The patient is first given a thorough bath with soap and hot water, the skin being well scrubbed to open the burrows. He is then placed in a cabinet, somewhat like a Turkish bath cabinet, seated upon a chair, with the head protruding through an opening in the top, and a warm, wet towel around the neck to prevent the escape of the vapor. A sulphur candle is then placed in the cabinet and lighted. After forty to fifty minutes the patient is quickly removed from the cabinet, and he puts on warm, clean clothing. The infected clothing and bedclothing may also be disinfected at the same time. It is important that the cabinet shall be warm and contain water vapor. In the majority of mild cases a single treatment is sufficient, the author having had but 2 per cent. of returns among 200 cases thus treated, and these he believed to be due to reinfection with insufficiently disinfected clothing. In the discussion which followed the reading of the paper, however, Major MacCormac called attention to the fact that the method was an old one which Hebra had tried and given up. MacCormac had found nothing superior to the old treatment, with sulphur ointment applied for three days after a preliminary hot bath.

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**Urticaria with Malaria.**—GARIN and PASQUIER (*Lyon méd.*, November, 1917) call attention to the great frequency with which urticaria occurs in connection with malaria. More than 30 per cent. of 135 patients under their care in the hospital for malaria at Modane suffered from recurring attacks of urticaria, and in almost every case the appearance of the urticaria was preceded by diarrhea. Jaundice of malarial origin was also frequently accompanied by urticaria, the association of these symptoms indicating a severe malarial infection.

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**Acanthosis Nigricans following Decapsulation of the Kidneys.**—WISE (*Jour. Cutan. Dis.*, January, 1918) reports a case of this rare malady following decapsulation of the kidneys done for mercurial



poisoning. The patient was a young woman who a year before had taken, with suicidal intent, a solution supposed to contain 7.5 grains of mercuric chloride. She was promptly treated and apparently made a complete recovery, but on the advice of friends, six days later submitted to decapsulation of the kidneys at the hands of another medical advisor. About nine months later she developed a severe dermatitis with intractable pruritus, which was followed by more or less general pigmentation of the skin, with masses of brown to black closely aggregated warty excrescences in the groins and axillæ; lichenification of the greater portion of the skin and moderate hyperkeratosis of the palms and soles were also present. The author believes the cutaneous disease to have been induced by some disturbance or impairment of function in the abdominal cavity brought about by the operation upon the kidneys.

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**Late Urticaria Pigmentosa.**—HARTZELL (*Jour. Cutan. Dis.*, November, 1917) reports two cases of urticaria pigmentosa beginning the one at twenty-three years of age, the other at nineteen, and calls attention to the increasing number of cases of this affection reported as beginning at or after puberty. Although the affection still remains practically a disease of infancy and early childhood it is probably much less infrequent in adults than has hitherto been supposed. Graham Little in a series of 142 cases collected from the literature and his own observations found no less than 14 per cent. beginning at or after puberty. While these late or delayed cases correspond in their symptoms in the main with the early ones, they also, in a considerable number of cases, have exhibited more or less marked departures from the typical cases. The adult cases have rarely shown lesions of the xanthelasmoid type. Attention is likewise called to the often insignificant role played by urticaria in the symptomatology and the consequent inappropriateness of the name by which the affection is known.

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**Focal Infection in the Etiology of Skin Disease.**—CHIPMAN (*Jour. of Cutan. Dis.*, October, 1917), in a paper read at the Forty-first Annual Meeting of the American Dermatological Association, arranges the dermatoses possibly due to focal infection in six groups: (1) Those related in some way with joint affections, such as erythema nodosum, erythema multiforme, gouty eczema, psoriasis; (2) those which apparently were more or less neuropathic in character, such as lichen planus, lichen simplex (Vidal), herpes simplex, herpes zoster, neurotic eczema, alopecia areata, dermatitis herpetiformis, scleroderma, vitiligo; (3) those related to tuberculosis as erythema induratum, lupus erythematosus, lupus vulgaris, lichen scrofulosorum, various tuberculides; (4) those arising from a focus in the skin itself, as impetigo contagiosa, infectious eczematoid dermatitis, various streptococic infections; (5) those having some relation to anaphylaxis, as eczema, urticaria, erythema multiforme, angioneurotic edema; (6) miscellaneous affections, such as rosacea, granuloma annulare, chilblains, Raynaud's disease. In a study of 50 consecutive cases of diseases belonging to these groups a very large proportion (49) showed infection of the teeth either alone or in connection with infection of the tonsils.

## PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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An Investigation of the Cultural Reactions of Certain Anaërobes Found in Wounds.—The confusion in our knowledge of the anaërobic bacteria is reflected in the literature, the expanding nomenclature and the divided opinions on the importance of the various strains isolated from wounds. The investigation of HENRY (*Jour. Path. and Bact.*, 1917, xx, 344) has resulted in a definite clarification of the subject and will undoubtedly serve as a stimulus to further work along the same general lines. The fundamental importance of pure cultures in such a study and some practical methods for isolation of the more important anaërobes found in wounds are well brought out. The method of isolation makes use of the author's modified M'Leod plate, attention being given to the special media and the careful technique found necessary, colony differentiation being practical after a little experience. Detailed descriptions of the more important anaërobes are given and methods of identification are clearly presented. The first and most frequently encountered is that of the *B. welchii* known under various names, viz., *B. aerogenes capsulatus*, *B. perfringens* (frequently used in the French and English literature), *B. phlegmonis emphysematosæ* of Fraenkel and a number of others. A subgroup, the *B. amylobacter* of Gruber and Bredmann, characterized by stormy fermentation of milk, in common with the *B. welchii*, and differing by its motility and the development of spores in milk, has not been found by the author in war wounds. The second group in point of frequency is the *B. sporogenes* (Metchnikoff). The name replaces *B. edematous maligni* of Koch so long in use for this active proteolytic group of anaërobes and since the term malignant edema may indicate a clinical but certainly not a bacteriological entity, it is very much better to use the simpler name. In this group should also be included the *B. putrificus* (Bienstock) and the *B. cadaveris sporogenes* of Klein. The vibrio septique of Pasteur, so often included in the group by earlier writers, is not placed here by the author, but rather in the saccharolytic group. The name *B. tertius* is that chosen by the author for the oval end spore-bearing saccharolytic bacillus which has been found as the third most frequent anaërobe of wounds. The other names used by various writers for this organism are *Bacillus ix* von Hibler, *Rodella iii* and *Bacillus Y* of Fleming. The author also includes in his study a number of anaërobes isolated and described by Weinberg and Seguin, viz., *B. fallax*, *B. aerofetidus*, *B. edematiens* and *B. histolyticus*. The fermentation reactions on a large number of carbohydrates is important and the author confirms the results of Simonds in the subdividing of *B. welchii*. In his discussion of the changes produced by anaërobes in the tissues the author points out the various conditions brought about in the wounds in modern

warfare, unavoidable, the soiling of the wound by earth or by clothing infected with fecal organism, the use of the short-range bullet and shrapnel shell, with the resulting extensive tissue damage. The anaërobes develop in damaged tissue just as they do in artificial cultures. The carbohydrate fermenters or saccharolytic group are the first to develop. The damaged muscle because of its carbohydrate content (about 1 per cent.) forms a favorable nidus for this growth. The glycogen of the living muscle is converted after death into dextrose and a small fraction of isomaltose, both of which are vigorously fermented by *B. welchii*. The author considers that the low sugar content in skin and subcutaneous tissue does not favor this development in wounds limited to these regions. The production of acid and gas results from this fermentation. The gas may appear clinically in four to six hours after the receipt of the wound and helps to embarrass the circulation. The organic acids bring about as one of the reactive changes an absorption of water by the protoplasmic colloids, and this combines with the exudate in the areolar spaces to form the edema so often seen in aërobic infections. This edema may spread far beyond the confines of the bacterial invasion. A second reactive change to the acid results in the appearance of autolytic enzymes both saccharolytic and proteolytic. The result of these various factors is a devitalization of the tissues. This early saccharolytic phase is followed in the wound, as in the test tube, by the proteolytic phase when the more slowly growing proteolytic group becomes established. The penetrating fetid odor so striking clinically in anaëroically infected wounds as well as the blackening of the tissue are both indications of the active presence of this second group. A third phase of toxemia and the last stage of anaërobic growth, the successful invasion of the blood, are rather briefly discussed. This article merits the careful attention of everyone interested in the bacteriology of war wounds. The illustrations are especially noteworthy.

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**Loss of Power to Produce Sarcomatous Transformation in the Stroma of Carcinoma.**—WOGLOM (*Jour. Cancer Research*, 1917, ii, 471) premises that certain changes which have been found in the stroma of carcinomata are sarcomatous. This is not a constant possession of the carcinoma cell, for the Flexner-Jobling tumor lost this power between the fifth and eleventh generations. Similar findings have been reported in four other tumors. The neoplasm described by the author was found in the left inguinal mamma of a female mouse of unknown age on March 17, 1914. The sarcomatous transformation of its stroma was lost after the fourth generation, and this power has not been regained up to the twenty-first generation. It recurred in one mouse in each of the first, second and fourth generations and in two mice of the third. The percentage of successful inoculations varied from zero to one hundred, and the growth was fairly rapid and usually continuous. The tumor type was an adenocarcinoma; alveolar areas were often encountered and keratinization was frequent. The stroma was not especially cellular. In the sarcomatous areas the characteristic halos of lightly stained cells encircling the cancer cells were seen. The author raises the interesting question "whether mouse tumors containing keratin may not, perhaps, induce sarcomatous development in their stroma more often than other types of carcinoma."

**Complement-fixation in Experimental Trypanosomiasis.**—It has been shown by a number of authors that the serum of animals infected with trypanosomes will give specific complement-binding with antigens prepared from the homologous trypanosomes or with certain organs of infected animals. Woods and Morris (*Jour. Infect. Dis.*, 1918, xxii, 43) studied complement-fixation with *T. equiperdum* with a view of determining the time of occurrence, the relation of the symptoms, its specificity and its relation to the Wassermann reaction, and to the effect of salvarsan. The antigen was prepared from the spleen tissue of infected rats. All of such antigens were not satisfactory because of the anticomplementary reactions. It was found that this antigen was as satisfactory as that prepared from the emulsion of the micro-organisms. Seven healthy dogs giving negative reactions with these antigens were infected with trypanosomes. The fixation reaction appeared in about eight days. The trypanosomes appeared in the blood before the reaction became positive. In only one animal did a positive fixation test precede the appearance of the trypanosomes. The fixation appeared to be specific. As the trypanosomes multiplied in the blood stream the sera of the dogs became anticomplementary. A variable and inconstant fixation of complement with the Wassermann antigen was also obtained. It was difficult to follow the effects of arsenobenzol treatment upon the fixation test because of the anticomplementary reaction. In one dog, however, treatment not only removed the trypanosome infection but also dissipated the anticomplementary and complement-fixation properties of the serum. The authors were able to demonstrate that by the addition of disintegrated trypanosomes to normal dog serum a moderate anticomplementary serum was produced.

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**Experimental Trypanosomiasis: *T. Equiperdum* Infection in the Dog.**—KRUMBHAR (*Jour. Infect. Dis.*, 1918, xxii, 34) in seeking for an agent to induce a slow destruction of the blood made use of the trypanosome which causes dourine in horses. This parasite he found was transmissible to dogs, inducing in them a fatal infection which, aside from his studies on blood destruction and regeneration, was of great interest. When once infected the blood of the dog readily transmitted the disease to new animals when given intravenously. There was an incubation period from three to eight days. With the appearance of the trypanosomes in the blood the animal showed weakness, loss of weight and progressive anemia. An irregularly disposed edema was not uncommon. Occasionally, also, eye lesions, such as keratitis, iritis and hemorrhages, were observed in the severe cases. Only twice were the manifestations suggestive of cerebral damage. With the appearance of the trypanosomes, signs of anemia manifest themselves both in the reduction of the hemoglobin and red cell count. The former may fall to 40 or lower while the latter is reduced to less than 3,000,000. A primary leukocytosis is followed by a leukopenia. Splenectomy was of no value in withstanding the infection. The author found that arsenobenzol was valuable in removing the infection and in bringing rapid improvement in the condition of the animal. They have found, however, that to ensure a permanent cure it is necessary to give three injections on successive days and to follow this with three or more injections at three-day intervals.

## HYGIENE AND PUBLIC HEALTH

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**The Etiology of Epidemic Poliomyelitis.**—E. C. ROSENOW, E. B. TOWNE, and G. W. WHEELER (*Jour. Am. Med. Assn.*, October 21, 1916, lxvii, No. 17) felt that a reinvestigation of the bacteriology of poliomyelitis by newer methods was desirable since Rosenow has shown by the use of special methods that the specific localizing power of bacteria is an important factor in the etiology of various diseases including those of the nervous system, and since Flexner and Noguchi found that the cultural conditions of the organisms with which they produced poliomyelitis in monkeys are "those that apply more particularly to the bacteria." A peculiar polymorphous streptococcus has been isolated often in large numbers from the throat, the tonsils, and from abscesses in the tonsils in a large number of cases of epidemic poliomyelitis. It has been obtained from the blood before and after death, from the brain and cord, and also from the intervertebral ganglia and lymph nodes in cases of this disease. The organism isolated produces on aerobic blood plates fine, dry, non-adherent, slightly green colonies, showing in forty-eight hours a narrow, hazy zone of hemolysis. On this medium and ascites-dextrose agar, the organisms are quite uniform in size but in ascites-dextrose broth, the organisms show polymorphous forms and in ascites-plain broth they are only about two-thirds the size. Old cultures show clumps of very small coccus forms. In a very few instances the early smears showed the tiny globoid bodies described by Flexner and Noguchi as present from cultures from tissues in poliomyelitis, but they also showed a number of medium-sized diplococci in chains which tend to grow smaller, so that at the end of twelve or fourteen days nothing but the tiny globoid bodies could be found. Transplants from these to another medium showed a marked tendency of the microorganisms to change their form according to the medium on which they were planted. Cultures of Berkefeld N. filtrate of emulsions of brain and cord of rabbits dead from paralysis following intravenous injection with suspensions of broth cultures of the large forms have grown into the characteristic polymorphous forms. In the liquid medium, during the early days of growth, chains are found which contain single members of all sizes and shapes. Paralysis with lesions in the central nervous system has been produced in guinea-pigs, rabbits, dogs, cats and monkeys by intravenous or intracerebral injection with this peculiar streptococcus in its large form from practically all of 52 cases of acute poliomyelitis. The incubation period in these animals was usually from three to five days.

The early paralysis were usually accompanied by evidence of pain in the affected extremity and the affected animals were apt to die within twenty-four hours of the onset. At necropsy the paralyzed animals showed hemorrhage and lesions in the brain and spinal cord, but noteworthy absence of these in other organs. In animals in which paralysis occurred early and which died soon after large injections, the large forms have only thus far been found, while in those which died after a long period of incubation, both large and small forms have been demonstrated. The same organism has been isolated from the brain and cord of paralyzed monkeys injected intracerebrally with fresh human virus of poliomyelitis. The authors state in conclusion "that the exact relation of our results to the facts already established as to the etiology of poliomyelitis cannot be definitely stated. It appears to us that the small filterable organism which has been generally accepted as the cause of poliomyelitis may be the form which this streptococcus tends to take under anaërobic conditions in the central nervous system and in suitable culture mediums, while the larger and more typically streptococcal forms which investigators have considered contaminations may be the identical organism grown larger under suitable conditions."

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**The Use of Insecticides against Lice.**—BACOT (*Brit. Med. Jour.*, September 30, 1916, No. 2909) made an attempt, in performing these experiments, to arrange the conditions on as nearly natural a basis as was possible. In order to test the relative effects of contact and diffusion of several insecticides, an apparatus was designed consisting of wire gauze frames which could each be covered by a small gauze bag; each constituted a series of five small cages so arranged that they could be tied against the skin. In the central chamber was placed a 1-inch square of thick lint saturated with the substance to be tested, and lice were placed in all five of the chambers. Several gauze bags containing no insecticides were included as controls, which were placed between the others to ensure no interference of the substances tested with each other's action. These tests were usually of eight to twelve hours' duration. The substances tested were naphthalene, sulphur, cresylic acid, iodoform, vermigelli, a prepared insecticide, combinations of this with phenol and cresylic acid, a mixture of vaseline, naphthalene, kerosene and benzole and pyrisine, an alkaloid having physiological properties similar to those of nicotine. The net results of these tests show that the diffusive effects of all the substances except possibly naphthalene is so slight as to reduce them all to contact remedies. Therefore, it is necessary to saturate or thoroughly dust underclothing with them to obtain any effect. If naphthalene is used in some form in which the garments can be impregnated with it, it is a very good insecticide and the chief objection which can be offered to it is the fact that it evaporates very rapidly. Tests were also made to investigate the effectiveness of remedies in preventing breeding when used to impregnate clothing. Flannel was saturated with the various remedies listed above, and the lice placed in contact with it for several hours in order that eggs might be laid and developed. In these tests an emulsion of soft soap and crude liquid carbolic acid was also used. This last was found to be the best remedy for impregnating clothing to prevent the spread of lice. Flannel was treated with the various remedies and, after two days, insects were placed in contact with it and the results noted.

In these tests also the emulsion of soft soap and carbolic was found to be the most effective, the practical effect of impregnation with it lasting about six or seven days and the smell have a slight effect for several days longer. Therefore a very practical insecticide for preventing the spread of lice among troops is an emulsion of 45 to 50 per cent. soft soap combined by heating with 50 to 55 per cent. crude carbolic. A 5 per cent. solution of the emulsion in warm water should be used to impregnate the garments, which should then be wrung and thoroughly dried before wearing.

**Spontaneous Amebic Dysentery in Monkeys.**—EICHORN and GALLAGHER (*Jour. Inf. Diseases*, September, 1916, xix, No. 3) describe a spontaneous outbreak of a disease in monkeys in which the lesions and protozoal organisms corresponded closely to those found in amebic dysentery in man. There is no record of any similar case, and there may be a possibility of transmission of the amebas to human beings and of animals being carriers of the parasites without showing any clinical evidence. In this outbreak 8 animals out of a total of 15 exposed succumbed, and of 9 developing symptoms only 1 recovered. These animals were spider monkeys, received at the National Zoölogical Park at different times from Central America. One of the monkeys was ill when it arrived, showing symptoms similar to those later manifested by the others. This animal died a month after arrival and in three months 8 of the other animals died of dysentery. The ameboid forms were especially numerous in liver abscesses but were also found in intestinal matter. They possessed motility for from twenty-four to thirty-six hours after the death of the animal in the liver specimens and then showed a tendency to assume a circular form, became more granular and smaller in size and appeared to be encysting. An attempt was made to transmit the disease to cats since it is generally understood that they are susceptible to *Ameba histolytica* but it was not successful, the cats remaining perfectly well. These experiments suggest that the parasite found is of a different species from that in man and is specific for the spider monkey. The cecum and colon were invariably the seat of pathogenic changes, the rectum being involved to a greater or less degree, and abscess of the liver was associated with the 2 cases showing the most extensive intestinal lesions. A study of the histological changes in the intestine showed ulceration of the mucosa but the other layers of the intestines were not greatly affected except in areas of deep ulceration. Microörganisms other than amebas were for the most part absent, as were the types of leukocytes usually present in microbial infections, and there was no pronounced congestion. In the liver tissue there were many necrotic foci varying in size and surrounded by amebas, and there was some congestion.

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ORIGINAL ARTICLES

SENSITIZED VACCINES IN THE PROPHYLAXIS AND TREATMENT OF INFECTIONS.

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A SENSITIZED vaccine is a suspension of bacteria which has been previously treated with an homologous serum. The administration of sensitized vaccine has sometimes been referred to as serovaccination or "combined active-passive immunization." Both of these terms are misleading: the former because the serum is removed by washing the bacteria before they are injected, the latter for the reason that the immunity produced is probably entirely active. Whatever antibody is present in the vaccine is firmly attached to the bacteria, and whatever value sensitization of a vaccine possesses probably inheres from the direct influence of the antibody on the bacteria to which it is attached.

Vaccination with a mixture of serum and vaccine has, of course, been tried by a number of investigators. Shiga<sup>1</sup> used such a mixture for immunizing against plague and dysentery. Calmette and Guérin<sup>2</sup> produced a considerable degree of protection against the bovine tubercle bacillus in cattle that had been inoculated with a mixture of bovine tubercle bacilli and immune (?) serum. Leclainche<sup>3</sup> has used this method for vaccinating against erysipelas.

<sup>1</sup> Deutsch. med. Wchnschr., 1901, xxvii, 741.

<sup>2</sup> Compt. rend. Acad. sc., 1910, cli, 32.

<sup>3</sup> Revue vétérinaire, 1900, xxv.



Sensitized vaccines in the true sense of the word were first employed in 1902 by Besredka.<sup>4</sup> He experimented with sensitized plague and typhoid bacilli which had been killed by heat, and found that the sensitized bacilli, both subcutaneously and intraperitoneally, were considerably less toxic than the non-sensitized bacilli; furthermore, that injections of sensitized bacilli were followed by an almost *immediate* increase in immunity, in contrast to the non-sensitized bacteria which excited first a so-called "negative phase."

In 1911 Metchnikoff and Besredka<sup>5</sup> succeeded in reproducing typhoid fever in chimpanzees by feeding them the excreta from a case of human typhoid fever. These investigators then experimented with various methods of vaccinating apes against typhoid. They found that killed typhoid bacilli, sensitized or non-sensitized, did not confer a sure and certain protection against typhoid fever in the chimpanzee. Living bacilli, however, if sensitized, produced a high immunity. The next experiment was to test the living sensitized bacilli on human beings. When one or two one-hundredths of a gelatin culture of living sensitized typhoid bacilli were injected subcutaneously a small area of erythema, slightly tender, developed at the site of the inoculation, but the temperature remained normal and the patient showed no untoward symptoms. In a later study the same experimenters showed that the blood and urine remained sterile even after large doses of living sensitized typhoid bacilli had been injected subcutaneously.

Besredka<sup>6</sup> has more recently reported his results with the use of living sensitized typhoid vaccine in human beings. On the island of Braqueville about one-half of the 930 inhabitants were vaccinated while the other half served as controls. During the year following four controls developed typhoid fever, while of those vaccinated all escaped infection.

In England, Broughton-Alcock<sup>7</sup> has used living sensitized typhoid vaccine in 750 cases for prophylactic purposes. His experience was similar to that of Besredka. A slight local reaction was obtained, but the temperature was rarely increased and other constitutional symptoms were entirely absent.

Sawyer<sup>8</sup> has recently reported the results of antityphoid vaccination in the State of California, and gives comparative figures for sensitized and non-sensitized vaccine. In the first place he found that there was little difference between the vaccines in regard to the severity of the reactions produced. Out of 2906 cases vaccinated with the sensitized vaccine 4.3 per cent. later developed typhoid; whereas in 4967 cases vaccinated with non-sensitized vaccine there was 6.9 per cent. of failures. Hence the percentage of failures indicates a slight advantage for the sensitized vaccine, though as the

<sup>4</sup> Ann. de l'Inst. Pasteur, 1902, xvi, 918.

<sup>5</sup> Ibid., 1911, xxv, 193, 867; 1913, xxvii, 597.

<sup>7</sup> Lancet, 1912, clxxxiii, 504; 1913, clxxxiv, 1155.

<sup>8</sup> Jour. Am. Med. Assn., 1915, lxv, 1413.

<sup>6</sup> Ibid., 1913, xxvii, 607.

authors point out, the two sets of statistics are not exactly comparable.

Gay and Claypole<sup>9</sup> have published an interesting experimental study on the various methods of prophylactic vaccination against typhoid infection in rabbits: (1) they found that unsensitized bacteria killed and precipitated by alcohol do not protect so well as sensitized typhoid bacilli treated in the same manner; (2) they showed that the alcohol-killed sensitized cultures protect almost as well as living sensitized cultures and that the sediment of alcohol-killed sensitized cultures gives a better protection than living sensitized cultures. Moreover, they found that the sensitized cultures produced little or no reaction in human beings. They recommend the dried ground sensitized sediment for vaccination against typhoid fever in human beings and give the three injections at two-day intervals in doses equivalent to 750,000,000 typhoid bacilli.

More recently the sensitized vaccine of Besredka has been extensively tried as a therapeutic measure in typhoid fever. Ardin, Delteil, Negre and Raynoud,<sup>10</sup> for example, employed it in 48 cases and had only one death (2.08 per cent.). Garbat<sup>11</sup> has reported his experience with sensitized typhoid vaccine in the treatment of 17 cases of typhoid fever. He concludes that in vaccinated patients the disease runs a milder course and complications are less frequent.

Ichikawa<sup>12</sup> reports a series of 82 cases of typhoid fever treated with living sensitized vaccine administered intravenously. There were 9 deaths (a mortality of 11 per cent.). The author claims that the usual mortality for this disease in the hospital where he worked was about 30 per cent. He also tried the vaccine subcutaneously on 23 cases, with indifferent results.

Gay and Chickering<sup>13</sup> treated 53 cases of typhoid fever with intravenous injections of a sensitized killed typhoid vaccine sediment prepared by the method of Gay and Claypole already described. The intravenous injection of the vaccine nearly always produced a chill, rise and fall of temperature and leukopenia followed by hyperleukocytosis. The injection of the vaccine was followed in a number of cases by the disappearance or diminution of bacteriemia and usually by an increase in the Widal. The mortality in this series was 9 per cent., or just about that of the best hospitals. In 66 per cent. of the cases a distinct benefit was obtained, as showed by lower temperature, disappearance or amelioration of subjective symptoms and an apparently accelerated recovery.

Although vaccination with sensitized virus has been mostly studied with the typhoid bacillus its use has not been confined to this organism. In both France and England sensitized gonococcus

<sup>9</sup> Arch. Int. Med., 1914, xiv, 671; Jour. Am. Med. Assn., 1913, lx, 1950.

<sup>10</sup> Ann. de l'Inst. Pasteur, 1913, xxvii, 644.

<sup>11</sup> Jour. Am. Med. Assn., 1915, lxiv, 489.

<sup>12</sup> Ztschr. f. Immunitätsf., 1914, xxiii, 32.

<sup>13</sup> Arch. Int. Med., 1916, xvii, 303.

vaccine has been extensively employed as a therapeutic measure with apparently gratifying results. Dopter and Pauron<sup>14</sup> found that gonorrheal arthritis and orchitis responded quickly to sensitized gonococcus vaccine. According to Broughton-Alcock, sensitized gonococcus vaccine was of no value in acute urethritis, but in arthritis, orchitis and epididymitis its effects were brilliant. Nicolle and Blaizot<sup>15</sup> have also obtained good results in gonorrheal infections with sensitized gonococcus vaccine.

Sensitized streptococcus vaccine was first employed by Levy and Hamm.<sup>16</sup> They treated 8 cases of puerperal fever with the autogenous bacteria, killed with carbolic acid and sensitized with a polyvalent streptococcus-immune serum. Six of the 8 cases recovered. Marxer found that sensitized streptococci killed with galactose were more efficient for protecting rabbits against streptococcus than were the killed unsensitized organisms. Broughton-Alcock has tried sensitized living streptococci as a therapeutic agent in impetigo, suppurative lymphadenitis, pyorrheas and sinusitis and claims to have obtained remarkable results. He sensitized the bacteria with a polyvalent antistreptococcus serum.

In 1910 Levy and Aorki<sup>17</sup> found that sensitized pneumococcus vaccine gave rabbits a higher degree of protection against the pneumococcus than ordinary vaccine and that its administration was not followed by a negative phase. According to their experiments the sensitized vaccine (killed by 0.5 per cent. carbolic) was less toxic than the non-sensitized, an observation in accord with that made by other observers in the case of various bacteria. As to its curative effect, it was absolutely useless if injected later than a few minutes after the administration of ten times the lethal dose. When the two were injected simultaneously some of the animals were saved.

Swift and Kinsella<sup>18</sup> have found that the serum of rabbits which have been injected with sensitized *Streptococcus viridans*, either dead or living, does not contain agglutinins, complement-fixation antibodies or protective antibodies. Similar results were obtained with sensitized vaccines of pneumococci, but sensitized living pneumococci showed a rapid production of antibodies.

Swift and Kinsella<sup>19</sup> have lately studied active immunization with sensitized pneumococci. In mice there was practically no difference in the degree of active immunity conferred by plain and sensitized vaccine. In guinea-pigs the sensitized vaccine was less efficacious than the plain. In rats there was also a higher degree of immunity in the plain vaccine series, but the immunity produced by the sensitized vaccine persisted longer.

These authors also show that animals may possess a high degree

<sup>14</sup> Bull. et mém. Soc. méd. des hôp. de Paris, 1913, xxxvi, 386.

<sup>15</sup> La Semaine Méd., 1913, xxxiii, 497, 595.

<sup>16</sup> München. med. Wehnschr., 1909, lvi, 1728.

<sup>17</sup> Ztschr. f. Immunitätsf. u. exper. Therapie, 1910, vii, 435.

<sup>18</sup> Proc. Soc. Exper. Biol. and Med., 1915-16, xiii, 103.

<sup>19</sup> Ibid., 1916-17, xiv, 120.

of active immunity and still show practically no antibodies in their serum, and they suggest that the immunity may be due in part to a tissue immunity.

Broughton-Alcock resorted to sensitized *Staphylococcus aureus* vaccine in a series of cases that had not responded well to unsensitized vaccine and obtained excellent results. He had the courage to employ a living vaccine, and in the earlier part of his work produced a number of abscesses at the site of inoculation.

Von Behring<sup>20</sup> has recently introduced a method of active immunization against diphtheria which consists in vaccinating human beings with a diphtheria toxin that has been neutralized with antitoxin.

A so-called "sensitized" tuberculin was first introduced by Fritz Meyer<sup>21</sup> in the form of a sensitized bacillary emulsion. Meyer found that (1) tuberculous animals could stand five times as much sensitized tuberculin as unsensitized; (2) that healthy animals could stand numerous injections of the sensitized vaccine, while they died after repeated injections of unsensitized tuberculin; (3) that healthy animals which could not be immunized with dead bacilli, developed so much resistance after a long treatment with sensitized material that a subsequent infection was much milder and ran a course six to eight times longer than the controls; (4) that freshly tuberculous animals by treatment with sensitized tuberculin got so much better that they could be looked upon as cured.

Meyer treated 47 cases of pulmonary and local tuberculosis with sensitized tuberculin, and of these 40 showed more or less improvement. The best results were obtained in the localized infections. In the pulmonary cases there was an improvement in the symptoms, but the signs in the chest and the bacilli in the sputum persisted. Citron<sup>22</sup> has also worked with sensitized tuberculin and looks upon it with favor. Both Meyer and Citron emphasize the mildness of the local reaction as compared with that of the usual bacillary emulsion.

During the past two years I have had some experience with sensitized vaccines, enough perhaps to justify a brief report of the results which I have obtained. I have employed sensitized vaccines of the typhoid bacillus, gonococcus, streptococcus, *Staphylococcus aureus* and tubercle bacillus. In the case of the typhoid bacillus the vaccine has been used only for prophylaxis, whereas with the other bacteria the vaccines were employed for therapeutic purposes. The technic of preparation of the various vaccines will be described separately.

1. SENSITIZED TYPHOID VACCINE. My experience with sensitized typhoid vaccine has been limited to 20 cases, in which it was used for prophylaxis. The vaccine was prepared from a stock strain

<sup>20</sup> Berl. klin. Wchnschr., 1914, li, 917.

<sup>21</sup> Ibid., 1910, xlvii, 926.

<sup>22</sup> Ibid., 1909, xlvi, 2288.

of *Bacillus typhosus* which had been under cultivation for several years in the laboratory. The bacteria were grown, as usual, on plain agar, washed off with normal salt solution, shaken, standardized and killed by heating at  $56^{\circ}$  for one hour. The killed bacteria were then treated with an excess of inactivated serum obtained from rabbits immunized against the homologous strain. The suspension was incubated in the water-bath for two hours, centrifuged, washed twice with normal saline and made up to the original volume. The dosage employed in all these cases was the same as that usually employed with ordinary typhoid vaccine, namely, 500,000,000 for the first inoculation and 1,000,000,000 each for the second and third. In 8 of the cases the vaccine was given at seven-day intervals; in the remaining 12 cases it was administered every other day, according to the method of Gay and Claypole. The latter method has the advantage in economy of time and seems to cause no unpleasant symptoms.

It will be observed that in this vaccine the bacteria were killed with heat, in this respect differing from that of Besredka and others who have used the living organism. It seemed to me that the slightly superior immunizing quality of the living vaccine was not a sufficient advantage to justify the risk involved in using the living organism.

The local reaction produced by the sensitized vaccine was always mild—less severe, I think, than that which usually follows an injection of ordinary typhoid vaccine. The area of induration and hyperemia was less extensive and the tenderness not so marked or persistent. The constitutional reaction was generally negligible. Occasionally a slight frontal headache or a feeling of lassitude was noticed a few hours after the vaccine was injected, but these symptoms soon passed away. One patient had a low grade of fever for several weeks after receiving the second inoculation and developed a slight cough and signs at the left apex. A diagnosis of pulmonary tuberculosis was made, though the tubercle bacillus was never found. She had been vaccinated against typhoid just one year previously. Under appropriate treatment she made a gradual but complete recovery.

The results of Gay and Claypole's experimental study of typhoid septicemia in rabbits give considerable weight to the presumption that in human beings sensitized typhoid vaccine would confer a higher immunity against typhoid fever than the unsensitized vaccine gives. This point, however, is at present incapable of final demonstration. It has been shown by Besredka and his co-workers that sensitized typhoid bacilli stimulate agglutinin formation to a less marked degree than non-sensitized bacilli, but that, on the other hand, phagocytosis and bacteriolysis are much more active after vaccination with the sensitized organisms.

The superiority of sensitized over non-sensitized typhoid vaccine in immunization against typhoid fever can be established only by an extensive use of the former and a comparison of the results with

those which have been obtained by non-sensitized vaccine. In the meanwhile the lesser toxicity of the sensitized vaccine and its possibly superior immunizing power are sufficient reasons for giving it a thorough trial.

2. SENSITIZED GONOCOCCUS VACCINE. I have employed sensitized gonococcus vaccine in 16 cases of gonococcus infection; gonorrheal vaginitis uncomplicated, 4 cases; vaginitis with endometritis, 1 case; vaginitis with salpingitis, 2 cases; vaginitis with arthritis, 2 cases; vaginitis with pregnancy, 2 cases; vaginitis, arthritis and pregnancy, 1 case; gonorrheal arthritis, 3 cases; gonorrheal epididymitis, 1 case. The gonococcus vaccine used was a stock vaccine prepared from the ten strains of the New York City Board of Health. The bacteria were cultivated on veal agar and sensitized in the living state with serum from a horse immunized against the homologous strains. The general method of preparation was similar to that employed in the case of typhoid vaccine, with the exception that the bacteria were not killed. They unquestionably died, however, very shortly after the vaccine was prepared, as they were suspended in salt solution which contained 0.5 per cent. phenol.

Of the 12 cases of gonorrheal vaginitis only 1 was an infant; the ages varied from three to twenty-nine years. By referring to Table 1 it will be seen that 2 of these cases were complicated by gonorrheal salpingitis and 2 others by gonorrheal arthritis. In every case the infection was several weeks or months old before vaccination was started. The inoculations were given at intervals of five to ten days; the average number of inoculations were nine, but 1 case received as many as sixteen. An interesting feature in connection with this series is the size of the doses. On reference to the table it will be seen that the dosage varied from 100,000,000 to 2,000,000,000, the former being usually the initial dose. These doses are, of course, much larger than those usually given of ordinary gonococcus vaccine. The reactions, as a general rule, were mild; in nearly every case the first inoculation excited a sharp local reaction, but the following injections rarely caused much inconvenience or pain. There was only one definite constitutional reaction, that was in Case 9, where after the second inoculation of 200,000,000 the patient had a headache and fever and was nauseated. Six of these cases recovered completely; 4 others showed improvement and they were lost sight of; the remaining 2 cases showed no improvement. It is difficult to say in these cases just how much benefit the patients derived from the vaccines, as they were receiving at the same time local treatment in the form of vaginal douches of potassium permanganate and weekly vaginal distention of 5 per cent. silver nitrate. These patients were not considered cured until vaginal smears were entirely free of gonococci and practically free of pus cells. In Cases 2 and 3 the vaginitis was complicated by pyosalpinx. In both these cases the local pain and tenderness subsided and almost disappeared during the course of the vaccine treatment.

TABLE OF CASES TREATED WITH SENSITIZED VACCINES.  
GONOCOCCUS CASES.

No.	Age, yrs.	Diagnosis.	Duration of infection before vaccine treatment.	Number of inoculations.	Dosage.	Character of reactions.	Other treatment employed.	Result.
No. 1	21	Gon. vaginitis	3 weeks	10	100 to 1000 million	Usually mild; one sharp reaction, after sixth inoculation	Five per cent. silver nitrate; vaginal distentions	Complete recovery; vaginal smears negative.
No. 2	29	Gon. vaginitis; gon. salpingitis	7 months	16	200 to 2000 million	Arm quite sore after first and second inoculations; other reactions mild	AgNO <sub>3</sub> vaginal distentions; iodo-baciline douche; ichthyol tampon	Complete recovery from vaginal discharge; smears and gonorrhea-fixation test negative; still slightly tender over right tube when last seen.
No. 3	21	Gon. vaginitis; gon. salpingitis	6 weeks	12	100 to 800 million	All mild	AgNO <sub>3</sub> vaginal distentions; potassium permanganate douche	Recovery from vaginal discharge; smears negative; disappearance of tenderness and pain over right tube.
No. 4	16	Gon. vaginitis; pregnancy	3 months	7	200 to 1000 million	Slight nausea after fourth dose; several sharp local reactions	AgNO <sub>3</sub> vaginal distentions	Successful delivery of child at full term during course of treatment; lost sight of; when last seen slight vaginal discharge but no gonococci.
No. 5	29	Gon. vaginitis	1 month	6	100 to 500 million	One severe reaction after fourth inoculation; others mild	Potassium permanganate douches	Recovered; vaginal smears negative.
No. 6	3	Gon. vaginitis	2 months	12	100 to 1200 million	Mild	Boric acid douches	Recovered; vaginal smears negative.
No. 7	23	Gon. vaginitis; gon. arthritis	Vaginal discharge 2 years; arthritis 3 months	2	100 to 200 million	Mild	Vaginal douches	Improved, slightly; lost sight of.
No. 8	28	Gon. vaginitis	12 months	15	100 to 2000 million	Mild	AgNO <sub>3</sub> vaginal distentions; vaginal douches	Recovered; vaginal smears and gonorrhea-fixation test negative.
No. 9	26	Gon. vaginitis; gon. arthritis; pregnancy	5 months	15	100 to 1000 million	Slight constitutional reaction after second inoculation; mild local reactions	Vaginal douches	Vaccine discontinued at end of eighth month of pregnancy; complete recovery from arthritis; practically no vaginal discharge; successful delivery one month later.
No. 10	22	Gon. urethritis; gon. vaginitis; gon. endometritis	11 months	8	100 to 500 million	Several sharp local reactions	AgNO <sub>3</sub> vaginal distentions; potassium permanganate douches	Improved; lost sight of.
No. 11	15	Abortion; gon. vaginitis	7 months	8	100 to 600 million	Several severe local reactions	AgNO <sub>3</sub> vaginal distentions; potassium permanganate douches	Slight if any improvement; irregular in attendance at clinic.
No. 12	18	Gon. vaginitis; gon. arthritis	9 months	7	100 to 100 million	Reactions generally severe	AgNO <sub>3</sub> vaginal distentions; potassium permanganate vaginal douches	No improvement; poorly nourished; general health poor; arthritis slightly better when last seen.
No. 13	35	Gon. arthritis (chronic)	2 years	5	100 to 300 million	Mild	Baking and massage	No improvement; patient lost sight of after fifth inoculation.

No. 14	21	Gon. urethritis; gon. arthritis	3 weeks	11	10 to 2000 million	Patient had sharp rise of temperature and was irrational for a short time after 2000 million dose	Baking and massage; first five inoculations were ordinary gonorrheal vaccine	Arthritis lasted three months; complete recovery.
No. 15	22	Gon. arthritis; gon. urethritis	2 weeks	16	30 to 1000 million	Mild	Baking and massage; prosthetic massage	Complete recovery after three months' treatment; first eight inoculations ordinary vaccine; last eight sensitized.
No. 16	21	Gon. epididymitis	11 days	11	200 to 1000 million	Mild	Suspensory and poultices	Recovery ten days after institution of vaccine treatment.

STREPTOCOCCUS CASES.

No. 1, C. L.	16	Chronic infectious endocarditis	3 months	11	100 to 800 million	Mild	Transfused once with blood from an immunized donor	Died from acute nephritis.
No. 2, H. L.	42	Chronic infectious alveolar abscess	Several months	6	5 to 50 million	Mild	First four injections were ordinary autogenous vaccine	Died.
No. 3, D. K.	22	Chronic infectious endocarditis	6 weeks	8	40 to 600 million	One constitutional reaction (?); others mild	None	Died; duration of illness three and one-half months.
No. 4, M. G.	24	Chronic infectious endocarditis	Several months	3	100 to 400 million	Mild	None	Died.
No. 5, T. K.	21	Acute cervical lymphadenitis; acute arthritis; streptococcus septicaemia	3 weeks	9	200 to 2000 million	One constitutional reaction following 2 billion dose	Sodium salicylate; aspiration and irrigation of knee-joint	Recovered after three months' illness.

STAPHYLOCOCCUS AUREUS CASE.

No. 1, Mr. K.	35	Furunculosis	1 year or more before sensitized vaccine was used	4	10 to 100 million	Mild	Surgical treatment when indicated	Permanent recovery.
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TUBERCULOUS CASES.

No. 1, A. G.	15	Tuberculous adenitis	Several months	15	0.000001 c.c. to 0.0007 c.c. S. B. E.	One sharp local reaction; several focal reactions	Fresh air; diet	Apparently complete recovery; glands disappeared.
No. 2, M.	49	Tuberculous adenitis (recurrence after operation)	5 years	18	0.000001 c.c. to 0.01 c.c. S. B. E.	Two sharp focal reactions	Staphylococcus aureus vaccine for discharging sinus	Glands disappeared; slight discharge from sinus has almost disappeared after Staphylococcus aureus vaccination.
No. 3, S. G.	7	Tuberculous adenitis	1 year	14	0.000001 c.c. to 0.0003 c.c. S. B. E.	Mild reactions	Eventual excision of glands	No improvement; one large gland became fluctuant; excision; recovery.
No. 4, B. D.	23	Tuberculous adenitis	10 years	10	0.00001 c.c. to 0.0005 c.c. S. B. E.	Mild reactions	Fresh air; diet; x-ray	Glands became smaller but did not disappear.
No. 5, V.	28	Tuberculosis of the vertebrae	5 years	2	0.0000005 c.c. to 0.000001 c.c. S. B. E.	Marked rise of temperature after both injections	Psoas abscess drained	Patient so sensitive to tuberculin that only the two injections were given; patient died a few months later.



**GNOCOCOCCUS EPIDIDYMITIS.** Sensitized vaccines have been used in only 1 case of gonorrheal epididymitis. Case 16 received his first dose of vaccine eleven days after the onset of the epididymitis. At that time swelling and pain were both marked. Three days later the swelling was much reduced and the acute symptoms had disappeared and a second dose was administered; three days later the swelling was gone and the testicle was practically normal. After two more inoculations the patient was declared cured. The only local treatment used was a flaxseed poultice and a suspensory.

**GNOCOCOCCUS ARTHRITIS.** Five cases of gonococcus arthritis were treated. Two of these were associated with gonorrheal vaginitis, 3 with gonorrheal urethritis. The first case of the gonorrheal vaginitis series (No. 9) had an arthritis of the right ankle. After five doses of vaccine the symptoms in the joint had entirely disappeared, though the vaginal discharge continued for some time after. In Case 14 there was polyarthritis following acute urethritis. This patient received several doses of ordinary stock gonococcus vaccine. After one month of local treatment and vaccination with stock vaccine, vaccination with sensitized vaccine was started. Large doses were given every five or six days, the largest being 2,000,000,000. After two months' treatment the patient was discharged free from symptoms. In Cases 7 and 13 the patients were lost sight of before the treatment was completed. The former showed improvement after two injections of vaccine; the latter felt no better after five injections. The fifth case (No. 12) of the gonorrheal series showed very little improvement of either condition; she was a poorly nourished, neurotic girl and was irregular in her attendance at the clinic.

In summarizing the gonococcus infections treated with sensitized vaccine, one received the impression that the vaccine has been of some benefit in most instances, but the results are no better than those obtained with ordinary vaccine. The 2 cases of vaginitis which failed to respond to treatment were both poorly nourished women of a type that never reacts particularly well to vaccine treatment of any kind.

**3. SENSITIZED STREPTOCOCCUS VACCINE.** I have employed sensitized streptococcus vaccine in 5 cases; 4 of these were cases of chronic infectious endocarditis; the fifth was a case of streptococcus septicemia. In all of these cases living autogenous streptococcus vaccine was used and the serum employed for sensitizing the bacteria was that of rabbits immunized against the homologous strain.

(a) *Infectious Endocarditis.* These were all typical cases of infectious endocarditis of several months' duration, and they all showed *Streptococcus viridans* in blood culture. Case 1 received in addition to the sensitized vaccine a transfusion from a donor who had also been inoculated with the same vaccine. The only effect

exhibited in any of these cases was a slight temporary reduction of temperature for two or three days following the injection, and even this reaction was not constant. All four patients died.

(b) The fifth case was one of *Streptococcus septicemia*, and is so interesting that I shall describe it in detail.

K. T., male, aged twenty-one years, student. Eight days before admission patient was suddenly taken with sore throat, headache, fever. Diagnosis: acute tonsillitis. After three days the sore throat subsided, but glands in the neck became swollen and tender. Patient was seen by Dr. Blake, who advised incision of the glands.

May 10, 1913. Glands incised by Dr. Blake; pus removed.

May 12. Temperature, 105°; chill, nausea, vomiting; blood culture shows a streptococcus which produces a slight hemolysis.

May 14. 200 c.c. antistreptococcus serum.

May 16. 25,000,000 autogenous streptococcus vaccine.

May 18. 50,000,000 autogenous streptococcus vaccine.

May 19. 175 c.c. antistreptococcus serum followed by a chill.

May 20. Blood culture *Streptococcus hemolyticus*; no signs of endocarditis.

May 25. 170 c.c. antistreptococcus serum followed by symptoms of anaphylactic shock and urticaria.

May 29. 200,000,000 autogenous living *sensitized* streptococci.

May 30. Temperature high and steady; patient moved to the country.

June 1. Pain in the right knee.

June 2. Signs of fluid in the right knee.

June 3. 400,000,000 sensitized vaccine given.

June 6. 100 c.c. cloudy, sticky fluid aspirated from the right knee.

June 8. Temperature, 105°; two chills; pulse poor; cultures from knee; *Streptococcus hemolyticus*.

June 10. 30 c.c. purulent fluid removed from joint.

June 11. Patient given sodium salicylate, 30 grains t. i. d.

June 13. Sensitized vaccine, 600,000,000.

June 16. Sensitized vaccine, 800,000,000.

June 17. Knee-joint irrigated with phenol solution, 1 to 80.

June 18. Chill; temperature, 106°.

June 20. Knee aspirated and irrigated; profuse sweating.

June 21. Knee aspirated; chill; temperature, 103°.

June 23. Chill.

June 24. Knee aspirated.

June 26. Knee aspirated; fluid decreasing and thinner.

June 27. 800,000,000 vaccine.

June 28. Knee aspirated; white blood cells, 14,200.

June 29. Knee aspirated; chilly; temperature, 104°.

June 30. Knee aspirated; 1 fluidounce removed; temperature, 105°.

- July 1. Knee aspirated.  
July 2. Vaccine, 1,000,000,000.  
July 3. Knee aspirated; temperature,  $99^{\circ}$  at 9 A.M.; no chill.  
July 4. Phenol, 1 to 120; temperature,  $99^{\circ}$  to  $100^{\circ}$ .  
July 5. One fluidounce removed; temperature,  $99.6^{\circ}$  to  $100.3^{\circ}$ .  
July 9. Aspiration discontinued; vaccine, 1,500,000,000; temperature normal.  
July 10. Temperature,  $102^{\circ}$ ; vaccine, 2,000,000,000 may have caused it.  
July 11. Temperature varied  $99^{\circ}$  to  $103^{\circ}$ ; no chills; pain in feet; rather nervous but condition good.  
July 18. 700,000,000 vaccines; no temperature; uneventful recovery.

The fact that is obvious from the study of these cases is that vaccines, even when sensitized, are of no value whatever in the treatment of infectious endocarditis.

The Streptococcus septicemia case was remarkable in that no focus of infection could be found. The tonsils became normal, the incision in the neck healed, but the blood culture remained positive for several weeks. There was no evidence of an endocarditis and the arthritis was obviously a metastatic process. The case was considered hopeless many times during the earlier part of the patient's illness. The interesting features of the case were: (1) almost continuously high temperature for two months; (2) failure of anti-streptococcus serum; (3) huge doses of living sensitized Streptococcus hemolyticus without severe reactions; (4) final recovery, including complete recovery of function in the suppurating knee-joint.

4. SENSITIZED STAPHYLOCOCCUS AUREUS VACCINE. I have tried sensitized Staphylococcus aureus vaccine on only one case. Mr. K., suffering with furunculosis, was treated with an ordinary autogenous Staphylococcus aureus vaccine, but without permanent success.

Several months later a sensitized vaccine was prepared and a series of inoculations was given, with the result that the furuncles disappeared and have never returned.

There seems to be some evidence that in cases of Staphylococcus aureus infection, where the patient is extremely sensitive to the organism, a sensitized vaccine may be effective where the ordinary vaccine has failed. Most patients can take Staphylococcus aureus vaccine without any unpleasant results, but I have on two or three occasions encountered cases in which very small doses of Staphylococcus aureus vaccine produced constitutional symptoms and a fresh outbreak of pustules or furuncles. Under such conditions I think the sensitized vaccine is indicated.

5. SENSITIZED TUBERCULIN. I have employed sensitized tuberculin in 4 cases of tuberculous adenitis, and in 1 case of Pott's disease. Of the 4 cases of tuberculous adenitis, 2 were in children and 2 in

adults. None of the 4 cases, so far as could be told, were complicated by pulmonary tuberculosis. Three of the patients improved; 1 showed no improvement. Two of the cases which showed improvement were cases that had been operated on for tuberculous adenitis and had recurrences of tuberculous glands. Under administration of sensitized tuberculin the glands in these 2 cases disappeared. The other case which improved was a very chronic one in an adult in whom there had doubtless been considerable formation of fibrous tissue in the glands. It is not to be expected that the glands in this case would entirely disappear. The case which showed no improvement was a girl, aged seven years. She received sensitized tuberculin over a period of five months. At the end of this time the glands were fluctuating and had to be excised. The patient with Pott's disease received only two inoculations of the sensitized tuberculin. Both injections caused such marked constitutional reactions that the treatment was discontinued. The patient had extensive tuberculosis and was in no way suitable for tuberculin treatment.

Sensitized tuberculin usually excites only a mild local reaction. Exceptionally in very sensitive cases the local reaction may be quite sharp. In Case 2 I recall one severe reaction which showed itself as a large purplish-red tender nodule of the size of a walnut which persisted for two or three weeks.

The patients were all started with 0.000001 c.c. and the dosage was gradually worked up, as with ordinary tuberculin, until the dose in one case was 0.01 c.c. Sensitized bacillary emulsion appears to have no advantage over the ordinary bacillary emulsion so far as therapeutic effect is concerned, but the local reaction is somewhat less severe. As a rule the sensitized emulsion produces a mild local reaction, whereas the ordinary bacillary emulsion often gives rise to rather tender subcutaneous nodules which very slowly disappear. In some instances, however, I have seen injections of sensitized emulsion produce similar nodules.

DISCUSSION. A great deal has been written during the past decade about vaccines, but in spite of this vaccine therapy still remains an empirical procedure. It has been repeatedly demonstrated that the injection of killed bacteria into a healthy animal calls forth the manufacture of various antibodies and that a state of immunity is thereby produced. The exact effect, however, of vaccination in the case of an infected animal or human being is not known, for the reason that no method has been worked out for studying the effect of vaccine in experimentally infected individuals. The expectations of Wright that the opsonic index would prove a reliable guide in the administration of vaccine have not been realized. At the present time the only guide is the condition of the patient. We do know that in a considerable number of cases the use of vaccine is followed by the improvement or recovery of the patient. The same may be said of sensitized vaccines. It has been maintained

by Besredka,<sup>23</sup> Barbat and Meyer,<sup>24</sup> Gay and Claypole,<sup>25</sup> and others that vaccination with sensitized typhoid bacilli produces a high grade of immunity, higher than that following the injection of non-sensitized bacilli. Furthermore, it has been demonstrated by Barbat and Meyer that sensitized vaccines excite a very active production of bacteriotropic bodies, while the agglutinins, bacteriolysins and complement-fixation bodies are stimulated very slightly if at all. On the other hand, the immunity attained by injections of non-sensitized typhoid bacilli is actively bacteriolytic and only slightly bacteriotropic in character. The explanation offered by Garbat and Meyer for these differences was that by means of sensitization the typhoid bacilli and their immune bodies (amboceptors) are combined so that when injected into an animal they are ready for immediate attack and destruction by the complement; whereas with the injection of non-sensitized bacteria the tissue cells must first elaborate the various antibodies before the bacteria can be sensitized (*in viro*) and broken up. Garbat<sup>26</sup> suggests that if the injection of ordinary vaccine causes a bacteriolytic reaction and the administration of sensitized vaccine a bacteriotropic response it might be advisable in prophylactic vaccination to inoculate individuals with both kinds.

By this same reasoning one can account for the lesser toxicity of sensitized vaccine, on the ground that sensitization renders the bacteria more susceptible to complement, and, accordingly, more capable of rapid disintegration into harmless products. It is, of course, important that sensitization of the bacteria should be complete. In order to make certain of this an excess quantity of a serum of high titer should be used and plenty of time allowed for the firm binding of bacteria with antibody. If there is not time to immunize rabbits some of the patient's blood may be withdrawn and the vaccine sensitized with the patient's own serum.

The question whether one should use a sensitized vaccine in the living form is an important one. With the *Streptococcus viridans*, *pneumococcus* and *gonococcus* the living sensitized virus (in my experience) is harmless when injected subcutaneously. With the *Staphylococcus aureus* I should be rather afraid of furuncles in spite of the work of Broughton-Alecock. With the typhoid bacillus one should not forget the recent work of Nichols. Nichols<sup>27</sup> has shown that Metchnikoff and Besredka's living sensitized vaccine produces a typhoid cholecystitis when injected directly into the gall-bladder of rabbits and is therefore infectious. Furthermore, he proved that rabbits cannot be successfully immunized with this vaccine against direct gall-bladder infection.

The increased time and labor necessary for the preparation of a sensitized vaccine naturally leads one to ask the question: Is the

<sup>23</sup> Loc. cit.

<sup>24</sup> Ztschr. f. exper. Pathol. u. Therapie, 1910-11. viii, 1.

<sup>25</sup> Loc. cit.

<sup>26</sup> Medical Record, 1916, xc, 1145.

<sup>27</sup> Jour. Exper. Med., 1915, xxii, 780.

superiority of sensitized vaccine sufficiently marked to justify such an expenditure? In the majority of cases, no.

In the case of the typhoid bacillus the sensitized living vaccine of Besredka is infectious and is capable of producing cholecystitis in rabbits. The local reaction produced by the sensitized vaccine is slightly milder than that caused by the non-sensitized vaccine, but the difference, after all, is inconsiderable. The figures of Nichols show that in practical use on patients there is very little difference in the protective power of the two. At the present time, therefore, we are hardly justified in giving up a well-tried agent like the non-sensitized typhoid vaccine and substituting a sensitized vaccine, the efficacy of which has not yet been thoroughly established.

My therapeutic results with sensitized gonococcus vaccine were not so brilliant as to impress me with their great superiority to the non-sensitized vaccine. My limited experience with sensitized streptococcus and staphylococcus vaccine does not allow of conclusions, but I should feel about these as about the gonococcus—that if sensitized vaccine was ever indicated it would be only after ordinary vaccine had failed.

I entertain some skepticism about sensitized tuberculin. Granted that the so-called immune serum could be produced (a rather generous concession) there would probably be considerable deterioration in the imported product, no doubt several months old, when purchased in the market. Of course the latter difficulty could be overcome by substituting a domestic preparation. This same product, "S. B. E.," has been used with tolerable success by A. C. Burnham.<sup>28</sup> As with other forms of tuberculin the results are not so good in pulmonary as in "surgical" tuberculosis.

**SUMMARY AND CONCLUSIONS.** It has been shown by numerous investigators that a vaccine sensitized with an homologous serum produces less local and constitutional disturbance when injected subcutaneously than does a non-sensitized vaccine. Even living virulent organisms when properly sensitized can be injected subcutaneously without serious consequences.

It has been maintained by some that sensitized bacteria, either living or dead, produce a more rapid and efficient immunity than non-sensitized bacteria do. This question, however, cannot be considered settled as yet.

Sensitized vaccines have been extensively used for prophylactic and therapeutic purposes.

The author has employed sensitized vaccines in a series of 47 cases, which include 20 cases of prophylactic vaccination against typhoid fever, and 27 cases of therapeutic vaccination against gonococcus, streptococcus, *Staphylococcus aureus* and tuberculous infections. The sensitized typhoid vaccine produces a somewhat

milder reaction than ordinary typhoid vaccine, and probably gives just as high an immunity. At the present time, however, the evidence for its superiority is not sufficient to justify the substitution of sensitized for ordinary vaccine in practice.

In the various infections treated with sensitized vaccines the results were, as a rule, no better than would have been expected with ordinary vaccine. It happened that in a few instances recovery followed the administration of sensitized vaccine after treatment with ordinary vaccine had failed. This may have been due to the fact that larger doses could be employed without untoward symptoms.

The chief objection to the general use of sensitized vaccines is the increased labor and time necessary for their preparation.

At the present time it would seem desirable to limit their use to the treatment of infections in which there is hypersensitiveness to ordinary vaccines or in which the latter have proved inefficacious.

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## A CHARACTER STUDY OF THE HEMIPLEGIC EPILEPTIC.

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IT has been a matter of frequent inquiry whether the so-called symptomatic or organic epileptic possesses the epileptic make-up or constitution,<sup>1</sup> and whether the mental stigma of his disease has any of the defects in primary instincts which are usually so obvious in idiopathic or essential epilepsy. While a study of the hemiplegic epileptic based upon infantile cerebral palsy and its attendant epilepsy cannot be considered as a strict criterion of the adult or organic group of epileptics, a study of such material may be considered as an earnest to the right approach to this symptomatic group of epileptics.

Several years ago Dr. Sharp and I undertook a study of the inheritance and presence of neurotic stigma in the families of the hemiplegic epileptics at the Craig Colony;<sup>2</sup> 433 cases of hemiplegic epilepsy were considered. We concluded that "the heredity factor in hemiplegic epilepsy is only a little less in evidence than that present in genuine epilepsy, and that the prognosis as to a sequential epilepsy following in the wake of a given case of infantile cerebral

<sup>1</sup> Clark: A Personality Study of the Epileptic Constitution, *AM. JOURN. MED. SC.*, 1914, cxlviii; see also *Clinical Studies in Epilepsy*, *Psychiat. Bull.*, January, 1916 to January, 1917.

<sup>2</sup> Clark and Sharp: The Role which Heredity Plays in Inducing Epilepsy in Children Suffering from Infantile Cerebral Palsy, *Jour. Nerv. and Ment. Dis.*, 1913, xl, 633.

palsy should be based upon the presence and degree of spasmophilia or neurotic history in any given case, and that this latter fact should be given as much or even more weight than the site, nature and degree of the initial cerebral injury expressed in the palsy."

In the foregoing statement as to the heredity factor in hemiplegic epilepsy, that the heredity in its frequency and degree runs almost if not quite parallel to that of essential epilepsy, it becomes doubly important for us to study the essential make-up of such individuals before the onset of their palsy as well as the symptomatic sequela of epileptiform attacks. To this end I have made a careful study of the make-up of a selected group of hemiplegic epileptics who are now, so far as their mental state is concerned, quite identical to those suffering solely from essential epilepsy.

The data summarized here are from 12 cases of hemiplegic epilepsy. The epileptic character was found in one side of the fraternity most frequently. Occasionally a high volatile explosive temper, combined with an intense egotistic self-centered and sensitive make-up, was present in both sides of the fraternity. From this actual small data the paternal parent was found invariably to be quick-tempered, while the mother and her family stock were usually mild and docile. In the whole material there were but 2 cases in which some marked degree of the epileptic make-up could not be found in the patient several years before the advent of the palsy or even from birth. The epilepsy seemed but a natural corollary made mandatory by the presence of a cerebral palsy in such children. Often enough several other children in the same family showed some degree of the same character. It would seem, however, that these siblings escaped epileptic reactions largely if not solely because their keen egotistic tendencies became fairly easily subordinated, or they socialized them, as most frequently obtains in other passionate-tempered and difficult children during early adolescence. Mental and physical characteristics similar to the hemiplegic epileptic were also possessed by the siblings of the same family, and in a few instances they continued to possess this type of make-up and had continued passionate outbursts of temper but no well-defined epileptic seizures occurred.

In brief, it may be said that (1) the hemiplegic epileptic has about the same neurotic inheritance as the essential epileptic; (2) he has also about the same degree of epileptic constitution before the onset of his palsy.

After the more or less certain advent of his epileptiform seizures the hemiplegic epileptic deteriorates physically and mentally more certainly and rapidly than his essential epileptic fellow. I have never known a hemiplegic epileptic to recover from his epilepsy, although in a few instances they have been immune from epileptic attacks for months, and in one instance of my own for more than a year. He is best conserved from rapid mental deterioration by a well-directed effort to maintain a proper mental hygiene and as wide and



intensive a field of interest as possible for one who has a paralytic handicap which is an added integral debit to his natural temperamental disability.

We have under study 12 hemiplegic epileptics between the ages of nineteen and thirty-five years, divided equally between the two sexes, all at present under institutional care.<sup>3</sup>

The majority of these patients (9) belonged to large families ranging all the way from three to nine members; one patient was an only child. In 5 cases they were the first born; in the others they were born between other children who were healthy and strong.

In 6 cases the father was dead, 3 of whom were described as having been "moderate drinkers." Two of the latter died of paralysis and Bright's disease. Other causes of death in the paternal parent were: progressive paralysis due to abscess; pneumonia; arteriosclerosis. In 1 case the mother was alcoholic and died of Bright's disease. Another died of mastoiditis. The other 8 were living and claimed to be healthy, with the exception of 1, who is now suffering from a form of insanity which did not develop until our epileptic patient was fifteen years old.

All of the patients under study were of normal birth, no instruments used, and were breast fed. Only 1 suffered from constipation as a baby. For the most part they were not very passionate as infants and were easily managed, with the exception of 3, who are described as crying and irritable.

The hemiplegia came on in one case after measles at eighteen months. In a second after diphtheria at three years; in a third and fourth after no sufficient cause at sixteen months and two years respectively; in a fifth after pneumonia at one and one-half years; in a sixth after a slight fall at twenty months; in a seventh after scarlet fever at six years; in an eighth after an attack of apoplexy at twenty-five years of age. In 3 cases the hemiplegia appeared to have been noticed on learning to walk, about the second year. In one case the hemiplegia came on at ten and one-half years, with no apparent cause; this latter patient's skull was opened and nothing abnormal was found.

In 8 cases the paralysis involved the entire right side and incapacitated the patient to a greater or less degree. In 1 case the right hand only was involved. Three cases showed a left hemiplegia. It is interesting to note in one of the latter cases the patient showed the typical epileptic constitution as shown in a study of the idio-

<sup>3</sup> In order to make this clinical study as accurate as possible, the same general precautions in collecting data were observed as those in my study of the *personality* of the essential epileptic. In addition, through the kindness of Dr. William T. Shanahan, superintendent of Craig Colony, to whom my best thanks are due, the case material was taken from that institution, and all were drawn from those admitted to Craig Colony from the New York City district. In this way I was able to gain as many interviews from relatives as were found necessary to make me sure of the data thus collected.

pathic epilepsies, but the epilepsy itself did not appear until her twenty-third year.

All were bright up to the time of the occurrence of the hemiplegia, and in some instances for many years after.

Probably due to a lack of observation on the part of the parents no petit mal attacks seem to have been noted before the onset of the grand mal epilepsy. In 2 cases only was there any record of there having been "dizzy turns" antedating grand mal attacks.

There are three distinct periods in which the onset of the grand mal epilepsy has a tendency to group itself in the cases under study; in very early childhood from eighteen months to three and one-half years; around adolescence from eleven to fourteen years; in 2 cases as late as the twenty-third and twenty-fifth year.

The descriptions given of the aura are for the most part very hazy. In 1 case there was "pain in the stomach;" another felt a numb sensation in the hand and felt very nervous five minutes before the attack; a third "felt irritable;" a fourth felt "dizzy;" another stated he felt "disturbed;" two others "felt the attack coming on" and called for assistance.

As stated all 12 cases are under institutional care and have been for several years. It is interesting to note that a half show little deterioration as yet. A few even show improvement, and these individuals are the ones who appear to enjoy colony life and have no inclination to return home, in most instances finding much more to keep them healthfully employed and interested there than in their former surroundings. The other half are gradually deteriorating mentally and physically; they are slower, their memory is becoming poorer and they show dissatisfaction and a lack of interest in their environment, and continually write to be allowed to return home.

A picture of the personality of the hemiplegic epileptic may be made up as follows, each characteristic having been considered separately and found to hold true in the majority of the cases studied.

The standing in school was, on the whole, rather poor; they were slow to grasp facts. They were quick and impulsive. Power of concentration and observation was fair. They showed good common sense and were self-reliant. There was almost a total lack of imagination and originality shown in play. There was only a slight tendency toward bashfulness and shyness. For the most part they were neat, clean and orderly, but not especially committed to routine. They played freely with other children, but as many showed a tendency to be domineering, they were not favorites among their playmates. They showed a tendency to be stubborn and difficult to handle before the onset of their epilepsy, and these characteristics became more marked after the epilepsy was in evidence. The majority were trustful and not suspicious, but nearly all were keenly sensitive, easily offended and saw slights when none were intended. A few patients showed a tendency to hold grudges. For

the most part there was a tendency for the hemiplegic epileptic to become more keyed up and irritable just before attacks, and after the attack had passed things would run smoothly for several days until "things began to pile up again."

There was a tendency toward assuming a pietistic attitude, but there was a lack of sincere religious zeal. They were frank and open toward the parents in a superficial degree. Half of the group under study were demonstrative and affectionate toward members of the family, while the other half showed a total lack of this trait.

Apparently, from the records, there were no exhibitions of tantrums before the epilepsy developed, a trait often seen before the advent of attacks in the idiopathic epilepsies.

They were neither overcourageous nor cowardly. Some were given to anxiousness and forebodings. As a rule they were truthful. A few were fantastic, but the majority were very matter-of-fact in their attitude toward life. There seemed to be little tendency to day-dreaming and castle-building, so far as the relatives were able to state. The general mood for the most part was one of over-seriousness, yet a few are depicted as being cheerful, happy and good-natured.

The hemiplegic epileptic has a very shallow grasp on anything in the intellectual field, and therefore likes to busy himself with various light duties, running errands, pulling weeds and various kinds of house and garden work, but they are incapacitated by their paralysis from doing manual labor in an efficient manner and show little ability to do anything well.

There have been various bereavements experienced by the patients studied, but only 2 have reacted keenly to the loss of a parent or near relative; for the most part there has been no deep reaction and little tendency to crave sympathy.

On the whole the mood is stable. There is a tendency to show more irritability and quick temper as the epilepsy advanced.

As a general rule the mother of the hemiplegic epileptic was found to be of the docile type, while the father was quick-tempered and easily aroused. Of the few cases recorded to resemble in physical or mental make-up one of the parents, there was a tendency to take after that parent who showed the liveliest temper.

Several of the group showed a desire to lead, but their playmates did not readily accede to their demand, and hence there were quarrels and feelings of jealous rage were engendered in the epileptic. Others of the group showed no tendency to dominate. A few liked to moralize and held others up to criticism, but did not care to be criticized themselves and had a tendency to blame others for their own shortcomings. They were fond of eating.

Unfortunately there seemed to be nothing in his environment from which the hemiplegic epileptic derived deep satisfaction. One liked to draw pictures, another liked to walk, a third was fond of

being well dressed; but aside from a very superficial interest in various things there was nothing from which they derived a soul satisfaction. In half of our group study, as the years passed, there was a tendency to deteriorate physically and mentally; the mind dwelled in the past while the memory content for recent events was hazy. The other half of our group managed to keep alive an interest in their colony existence and were able to inject themselves into their environment, and these are the type of individuals who showed less tendency to deteriorate; the onward march of the disease seemed to be held in abeyance, while one or two are said to even show improvement.

In conclusion one may say that epileptiform attacks following in the wake of infantile cerebral palsy are not dissimilar in their final results to those of a frank and enduring essential epilepsy. They have about the same degree of heredity as their idiopathic congener, and there is present about the same degree of personality make-up in the individual who suffers from it. A more extensive study along the same general lines should be made, and, finally, the same painstaking investigation ought to be made upon epileptics who are supposedly made so by other cerebral insults of adult life. There are reasons, as well as some data already collected, to show that this latter material will disclose not dissimilar results to those shown in this small study of infantile cerebral hemiplegic epilepsy.

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## STUDIES IN FRACTIONAL ESTIMATION OF GASTRIC CONTENTS.

### II. EFFECTS OF ANTACID MEDICATION ON GASTRIC ACIDITY AND SECRETION.<sup>1</sup>

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THE effect of antacid medication, particularly the alkaline salts, upon the human and the animal stomach is still a matter of dispute. The general impression of those who are not familiar with this issue is that the alkali acts as a specific antagonist to the acid secretion of the stomach, neutralizing the acid and thus satisfactorily reducing the hyperacidity. This was the empirical basis upon which, for

<sup>1</sup> This study was accomplished under the tenure of a George Blumenthal, Jr., Fellowship in Pathology.

many years before the birth of the present-day experimental medicine, the antacid qualities of the mineral springs of Vichy, Ems, Carlsbad and other resorts were so warmly recommended by the profession as a cure in gastric disorders of the hyperacid type. Jaworski,<sup>2</sup> an enthusiastic defender of the efficacy of the Carlsbad waters, stated, in 1888, that the alkaline properties of these waters caused an atrophy of the secreting tubules and converted hyperchlorhydria into hypochlorhydria. This effect was supposed to be carried to the point of setting up a gastric catarrh, associated with a diminution of the acid supply. Much apparent support was lent to this view by the experimental work of Pawlow,<sup>3</sup> Bickel,<sup>4</sup> Heinsheimer,<sup>5</sup> Rosenblatt<sup>6</sup> and others. As an example of the best type of experiment upon which such a view was founded one needs but read the results of Pawlow. A dog with multiple fistulæ was fed meat saturated with bicarbonate of soda. As a result Pawlow<sup>7</sup> noted a diminution of all the alimentary secretions, gastric, salivary, pancreatic and intestinal, and a definite delay in the emptying time of the stomach.

However the doctrine of the inhibitory action of the alkalis on acid production was not to go unchallenged; an immediate protest was noted on the part of the clinicians. They attempted to control, by repeated test meals on patients suffering from hyperchlorhydria, the animal experiments as carried out in the laboratory. The contradiction of the laboratory findings by the bedside conclusions of the clinicians was striking. Du Mesnil,<sup>8</sup> feeding to a patient increasing doses of alkali (soda bicarbonate), found, as a result, on successive days an increasing daily acidity. Von Leube<sup>9</sup> held that bicarbonate of soda, although neutralizing temporarily, gave rise to a secondary stimulation of the acid secretory glands. The most striking refutation was offered by Linoissier and Lemoine,<sup>10</sup> who utilized a subject of merycism for repeated experiments to establish the therapeutic efficacy of bicarbonate of soda. Their results are given in the following words: "The immediate effects of bicarbonate of soda on gastric secretion are excitant whatever the dose. The first effect of the excitation is to saturate or neutralize the acidity if the dose is weak or moderate; an augmentation of the chyme and hydrochloric acid is produced. If the dose is massive, neutralization is attained, following which an arrest of hydrochloric acid production may occur, but before the normal acidity

<sup>2</sup> Wien. med. Presse, 1888, xxix, 87.

<sup>3</sup> The Work of the Digestive Glands, 1910.

<sup>4</sup> Berl. klin. Wchnschr., 1905, xliii, 869.

<sup>5</sup> Med. Klin., 1906, ii, 616.

<sup>6</sup> Inaug. Dissert., Berlin (quoted from Boas: Diag. und Therap. der Magenkrankheit, sixth edition, 1912, p. 351).

<sup>7</sup> The Work of the Digestive Glands, 1910, p. 232.

<sup>8</sup> Deutsch. med. Wchnschr., 1892, xviii, 1112.

<sup>9</sup> Ziemssen's Handbuch Therap., 1874, vii, 220.

<sup>10</sup> Bull. gén. de therap., 1894, cxxvii, 492.

is reached the food may have left the stomach." Further, they saw at Vichy an anacidity case converted into one of hyperacidity by drinking of the alkaline waters of the spring. Bourget,<sup>11</sup> by careful observations in his clinic, using the method of successive test meals, was fully convinced that the alkalis caused an eventual augmentation rather than diminution of gastric acidity.

And yet the issue between the research workers in the laboratory and the clinicians was not clear cut; contradictory testimony to both views was not lacking. Claude Bernard,<sup>12</sup> the distinguished physiologist, distinctly stated as early as 1879: "En faite, on sait tres bien que le suc gastrique s'ecoule en plus grande abondance quand on introduit des alcalines dans l'estomac; les acides au contraire, entrarent sa formation."<sup>13</sup> Mathieu and Laboulais,<sup>14</sup> using the repeated test-meal method on human subjects, found conclusions contrary to those of the body of clinicians, observing a diminution of hydrochloric acid production both after immediate alkali administration and after the prolonged use of alkalis therapeutically.

The standard modern text-books on pharmacology and therapeutics reflect the views of these two opposing schools of observers, without adding any testimony which would tip the scale in favor of either one.

**PERSONAL EXPERIMENTS.** In a previous paper it was suggested that the method of fractional estimation of stomach contents offered many new facts regarding the course of human digestion and the cycle of chemical activity. The method lends itself as a means toward the further investigation of the action of drugs and diet upon the secretion of the stomach. Introduced by Schuele<sup>15</sup> and Ehrenreich,<sup>16</sup> and recently elaborated and extended by Reh fuss,<sup>17</sup> the fractional test is an ideal one for further experimentation on such a subject. By allowing of the withdrawal of specimens of chyme at short intervals throughout the duration of digestion it offers the opportunity of charting the variations in the secretion of acid and ferments, also of observing the emptying time of the organ. Further, one is enabled to note the effect of drugs on the reflex flow of duodenal contents and of the secretion of gastric mucus.

The method employed in the following experiments is identical with that used in the previous publication. In the former paper<sup>18</sup> the deviation from the normal of the various factors incident to disease was ascertained and studied. The experiments in this

<sup>11</sup> Die Krankheiten des Magens und Ihre Behandlung, 1906, p. 90.

<sup>12</sup> Leçons de phys. oper., 1879, p. 570.

<sup>13</sup> "Actually, one notes an abundant secretion of gastric juice upon the introduction of alkalies into the stomach; acids on the contrary arrest its production."

<sup>14</sup> Bull. et mém. Soc. méd. d. hôp. de Paris, 1894, xi, 615.

<sup>15</sup> Ztschr. f. klin. Med., 1895, xxviii, 461.

<sup>16</sup> Ibid., 1912, lxxv, 231.

<sup>17</sup> AM. JOUR. MED. SC., 1914, lxi, 11.

<sup>18</sup> Crohn and Reiss: AM. JOUR. MED. SC., 1917, cliv, 857.

study were performed on the emptied fasting stomach in the morning. A heavy oatmeal gruel was utilized as the test meal. Specimens of chyme were withdrawn every fifteen minutes until the viscus was again empty, as evidenced by the failure to obtain further specimens. The motility of the organ was adjudged by noting the last specimen to give the starch reaction with iodine. The regurgitation of bile was carefully observed, as was also the presence of the heavy, ropy mucus characteristic of the pyloric mucous secretion. In every case, on one or more days previous to the experiment, a control curve without medication was plotted.

The patients upon whom the experiments were made were all cases of mild functional disturbances; individuals with definite organic lesions were not included. The majority of the experiments were performed on patients with isosecretory or hypersecretory types of curve except when otherwise stated in the text. Illustrative single examples are described in the paper; each individual experiment was, however, sufficiently controlled by frequent repetitions, often on different patients.

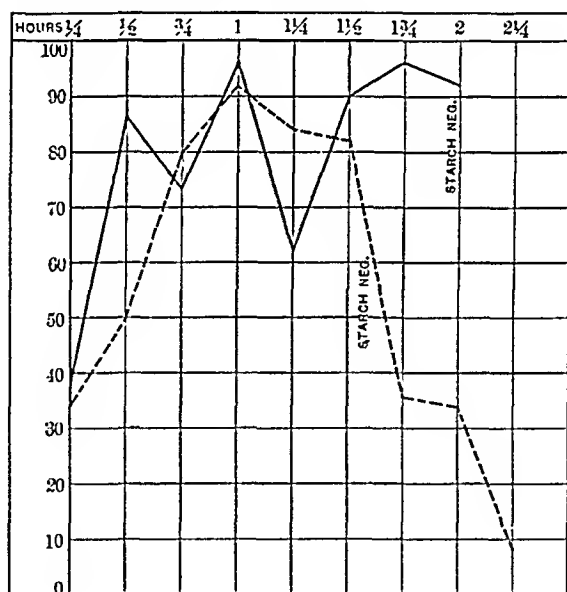


FIG. 1

EFFECT OF ALKALIES ADMINISTERED TO THE FASTING STOMACH BEFORE A MEAL. Magnesium oxide (calcined magnesia) was employed in this experiment and was administered in 1-gram dose one-half hour before the test breakfast. The effect was at once apparent (Fig. 1). An acid curve which reached its height (94 per cent.) at the end of one hour and then gradually fell to zero, was converted into a curve in which the maximum height (86 to 96 per cent.) was achieved at the end of the first half-hour

and was maintained practically constant at this level to the end of digestion. In other words a mild hyperchlorhydria existing for three-quarters of an hour during the height of digestion was converted into a hyperchlorhydria of greater degree and maintained as a constant for one and three-quarter hours. Numerically expressed, an average total acidity of 55.6 per cent. had been converted into an average total acidity of 78 per cent. In the control experiment the stomach was free of starch one and a half hours after the introduction of the test breakfast; after the administration of the magnesia the final emptying was delayed to two hours after eating. In the control experiment a beneficent regurgitation of bile marked the decline of the acid curve; in the instance with magnesia this was not observed.

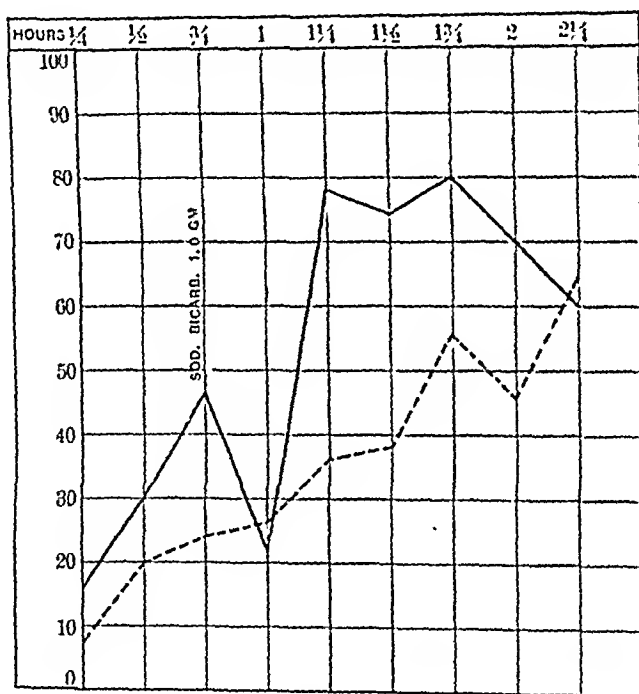


FIG. 2

EFFECT OF ADMINISTRATION OF ALKALIES IN SINGLE DOSE DURING DIGESTION. Bicarbonate of soda in 2-gram dose (30 grains) was given to a patient three-quarters of an hour after the onset of digestion. In fifteen minutes the acidity dropped from 46 to 22 per cent.; within another fifteen minutes it had rebounded to 78 per cent., which level it maintained for one-half hour and then slowly declined (Fig. 2). Numerically expressed, an average acidity of 43.6 per cent. in the control test was converted into an average acidity of 64 per cent. upon the administration of 2 grams of bicarbonate of soda. The total depression of acidity following the taking of the salt was for the duration of one period only, or fifteen minutes; the secondary augmentation of acid was for the



duration of the entire remaining portion of the digestive cycle. No delay in motility was noted in this instance.

On administering to another patient twice this dose of bicarbonate of soda (4 grams—60 grains) the reaction of the stomach to the alkali was so rapid that the very first specimen of chyme withdrawn fifteen minutes after the exhibition of the bicarbonate showed an increase in the acid titer. This demonstration of the evanescent action of sodium bicarbonate is occasionally confirmed by the personal experience of those who have employed this salt for the relief of heartburn or hyperacidity.

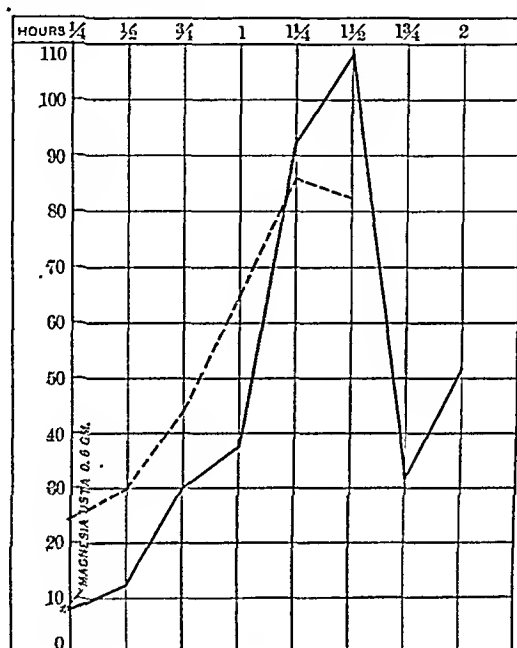


FIG. 3

Magnesium oxide (calcined magnesia) was chosen as the type of more slowly acting, but more efficient alkali. In an experiment in which it was administered directly after eating, in dose of 0.3 gram (4.5 gr.), it caused a negligible diminution of acidity (34.6 to 32.2 per cent.). The emptying time of the stomach was, however, delayed; in the control test it was one and three-quarter hours, in the test after medication it was two and a half hours. The delay in motility was attributable to the rise in acidity late in the course of digestion. As in the previous experiment with bicarbonate, one noted the absence of the bile which normally regurgitate as the acidity falls toward the end of the secretory activity.

Upon doubling the dose of the magnesia (0.6 gram or 9 grains) to another patient the average total acidity was decreased from

54.6 per cent. without medication to 46.5 per cent. after the magnesia, but the curve of acid secretion was completely disfigured. Following the administration of the alkali a maximum acidity of 86 per cent. in the control test was converted into a hyperacidity of 108 per cent., thus again affording an illustration of the unfavorable reaction of the gastric mucosa to the presence of alkalis. The resultant curve is illustrated in Fig. 3. The motility was slightly delayed.

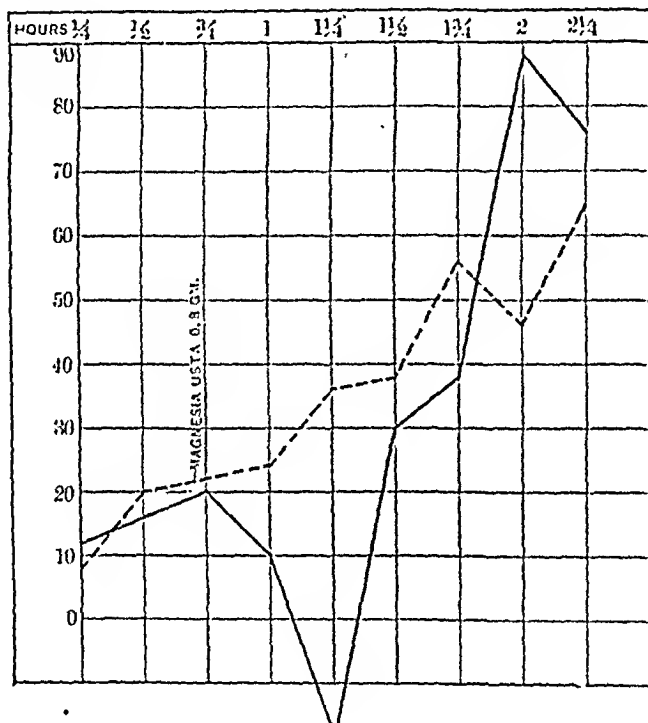


FIG. 4

To a third patient magnesium oxide 0.8 gram (12 grains) was given. The drop in acidity was less rapid but more prolonged and of greater magnitude than in the bicarbonate series. Thus in the first fifteen minutes after the medication the acid titer fell from 20 to 10 per cent.; in the next period it fell from 10 per cent. acid titer to 5 per cent. alkaline titer, a total fall of 15 per cent.; however, in the course of the next three periods or forty-five minutes an irritative reaction on the part of the stomach was observed. The acid titer rose rapidly to 26 per cent., then to 38 per cent. and finally to 88 per cent., exceeding at this point the maximum acidity in the control test by 24 per cent. (Fig. 4). It was evident that what had been gained by the initial neutralization was more than compensated for by the subsequent increase in acidity. The average total acidity was decreased from 40.6 to 34.6 per cent.

EFFECT OF ADMINISTRATION OF ALKALI AT END OF TEST MEAL. A dose of magnesium oxide, 0.8 gram (12 grains), given one and three-quarter hours after the ingestion of the test gruel, caused a rapid and efficient neutralization of the digestive acidity without secondary rise (Fig. 5).

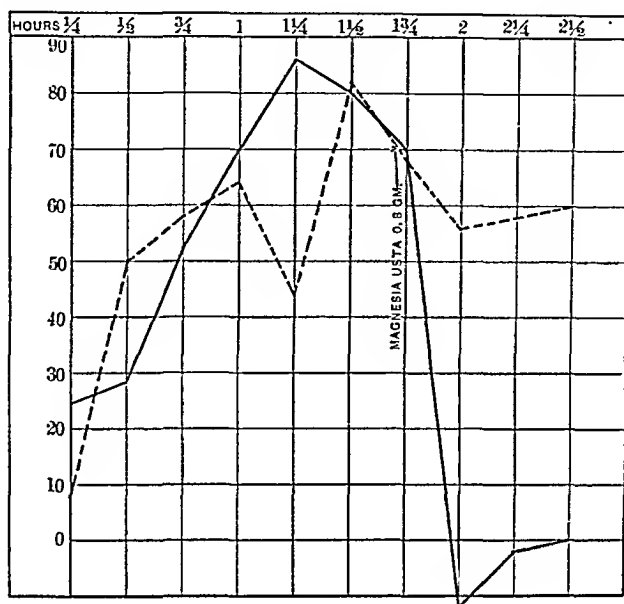


FIG. 5

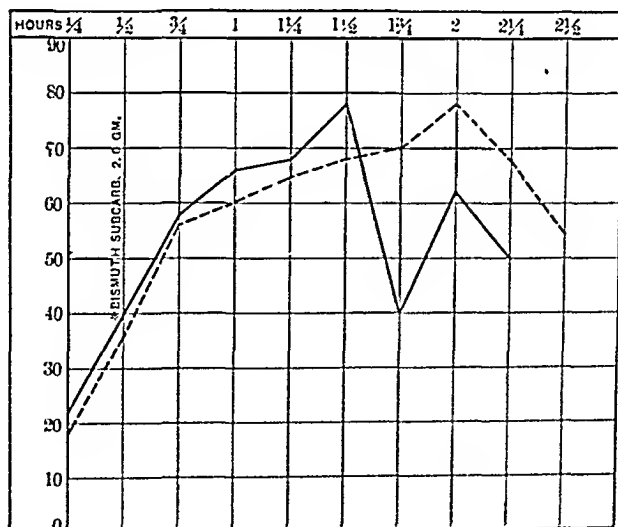


FIG. 6

ANTACID EFFECT OF BISMUTH SUBCARBONATE. The resultant curve, occurring from the administration of bismuth subcarbonate

in 2-gram dose directly after the meal, was obtained. A diminution of acidity was observed to take place without a corresponding compensatory increase in the acid secreted. The total depression of the acid was almost 50 per cent.; a very slight prolongation of motility was observed. The neutralizing action of the bismuth salt was efficient, moderate and prolonged and without deleterious after-result. In a duplicate experiment on another patient using a slightly greater dose the acidity was depressed from 56.8 to 45.2 per cent., without delay in motility or secondary reaction (Fig. 6).

**KAOLIN: ACTION OF AN INERT MINERAL EARTH ON GASTRIC ACIDITY.** This substance was chosen in an attempt to estimate the adsorbent power of an inactive mineral matter. No effect was apparent.

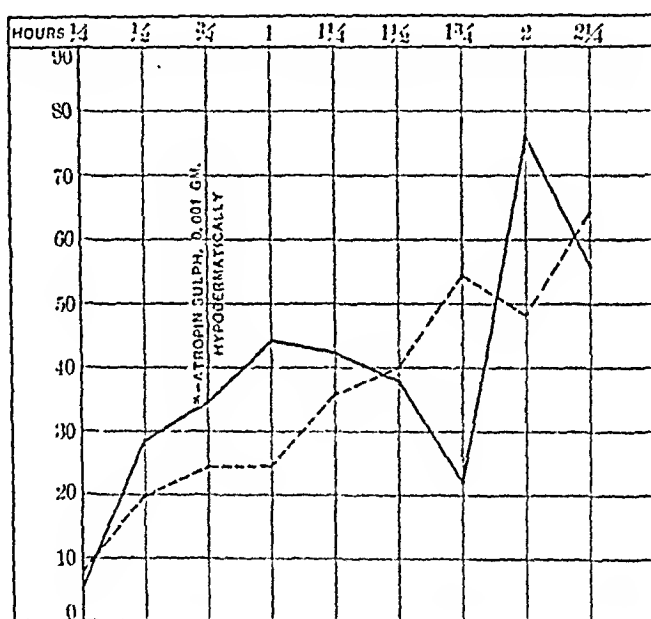


FIG. 7

**ATROPIN: ITS EFFECT ON GASTRIC SECRETION AND MOTILITY.** A patient whose control curve had been previously ascertained was given 1 mg. of atropin ( $\frac{1}{60}$  grain) hypodermically three-quarters of an hour after the ingestion of the test gruel. Little or no result was seen, except that in the last half-hour there was a rapid rise of acid from 32 per cent. to a maximum of 76 per cent. No diminution of acidity was observable at any time; in fact, there was a slight rise of average total acidity (35 to 38.6 per cent.) (Fig. 7). Motility was unaffected. A similar experiment in another patient gave practically identical results.

In the hope of obtaining a better result by the prolonged administration of this alkaloid the former patient was fully atropinized by the taking of moderate doses of atropin by mouth for several days. A fractional estimation made at this time failed to exhibit

the slightest variation from the control curve (Fig. 8). The average acidity had increased rather than diminished, namely, from 35 to 51.1 per cent. Motility was unaffected. The patient was showing at the time of the experiment the signs of early belladonna poisoning, that is, dilated pupils, dry mouth, etc.

**ATROPIN: ITS EFFECT ON CASES OF HYPERSECRETION.** The previous experiments were performed upon patients with iso-secretory curves or on those showing only slight hyperacidity. The pharmacological action of belladonna is that of diminishing secretion. It was therefore of interest to observe the effect of the atropin in cases of hypersecretion both as regards the effect upon the acidity as well as upon the secretion of the watery, gastric juice characteristic of the disease. The following conclusions are based upon experiments with two cases of hypersecretion:

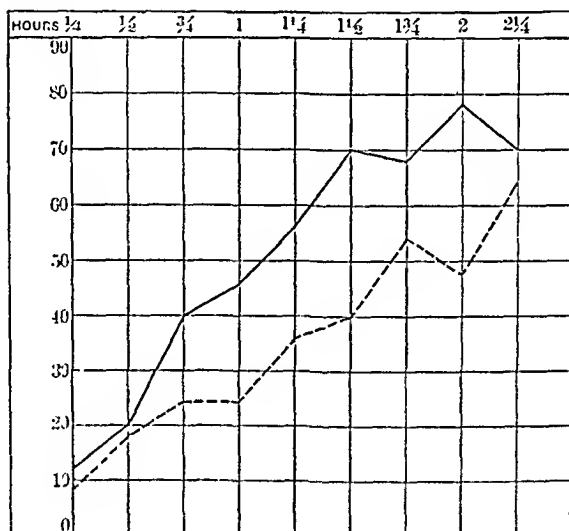


FIG. 8

The first case was one of functional hypersecretion of the continuous type, so-called Reichmann's disease. An exploratory laparotomy had failed to show any organic lesion. Upon administering the usual gruel test meal a highly acid gastric juice was secreted which continued as long as observed (six and three-quarter hours). All food had left the stomach after two and three-quarter hours, and yet the secretion continued. An average total acidity of 89 per cent. was estimated. The test was repeated on a succeeding day; after two and one-quarter hours the stomach became free of the last traces of the oatmeal gruel; the hypersecretion continued. At this point the patient was given by hypodermic 1 mg. of atropin ( $\frac{1}{100}$  grain). Within an hour the secretion had

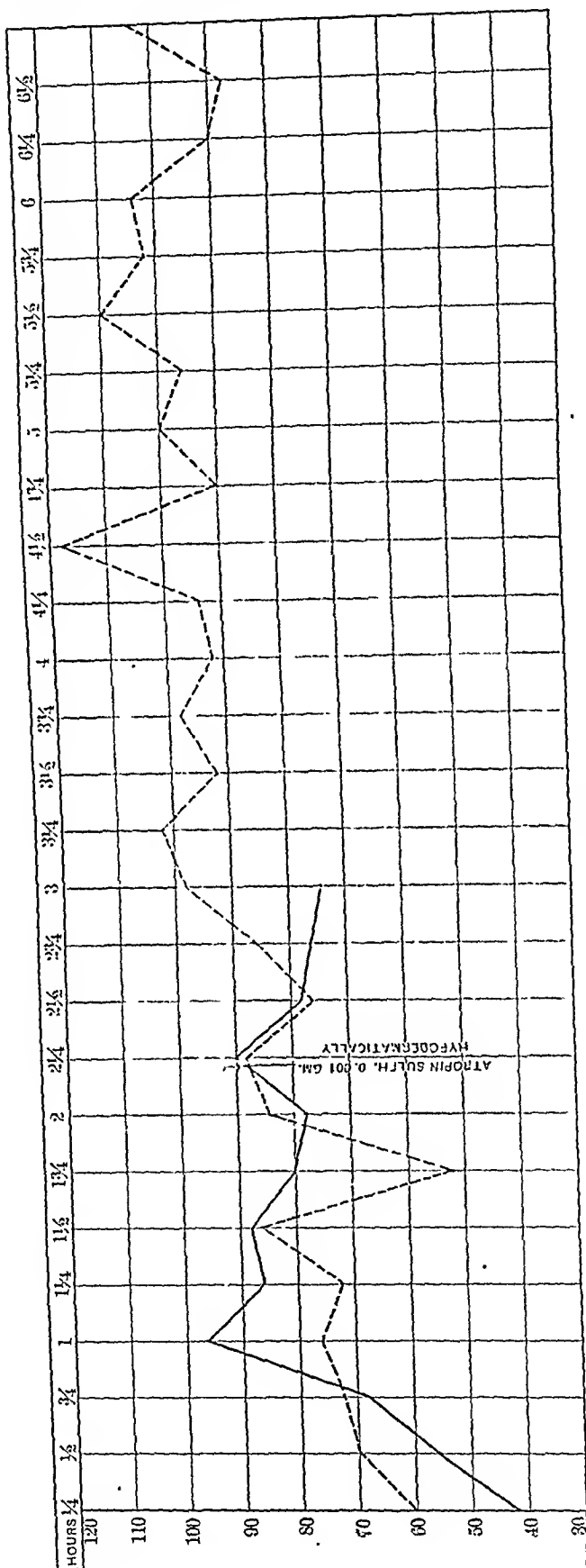


FIG. 9

ceased, the total acid titer diminishing gradually to 56 per cent. The patient was thereupon fully atropinized by being put on atropin sulphate by mouth in large doses for three days. A fractional test made at this point showed a delay in motility to three hours, but the secretion ceased three and one-half hours after taking the test meal. The average total acidity was reduced to 60 per cent. (control, 89 per cent.).

In the second case of continuous hypersecretion the secretion of acid juice lasted five and one-half hours or more after the ingestion of the test meal; the average total acidity was 85.3 per cent.; emptying time was three and one-half hours. On a subsequent day atropin sulphate 0.0012 gram ( $\frac{1}{50}$  grain) was injected hypodermically one-half hour before the test meal was given. The effect was very striking. Secretion ceased after two and one-quarter hours; acidity was reduced to an average total acidity of 47.3 per cent. Motility was improved, the stomach emptying in two and three-quarter hours.

While the result in this case of atropin administered hypodermically before the meal was very effective in reducing both the hypersecretion and the hyperacidity, yet it was recognized that for continuous usage such a method was not practical. Therefore after an interval of a few days the experiment was repeated, except that the atropin in identical dose was administered per oram. The result was disappointing, the hypersecretion continuing for seven hours and the average total acidity being raised from 85.3 per cent. in the control to 90.4 per cent. in this test. The motility was unaffected.

The patient was now given 1 c.c. of tincture of belladonna four times a day, this being continued for three days until the physiological results of the drug began to manifest themselves. A fractional test made at this time showed an increase of average total acidity from 85.3 to 104.5 per cent., but a diminution of the duration of the hypersecretion, the latter ceasing after three hours.

**OLIVE OIL: DOES IT AFFECT GASTRIC ACIDITY?** Two ounces of olive oil were administered to a patient whose control curve had previously been ascertained. The resultant figures were disappointing in that a slight rise rather than a fall of total acidity resulted, namely, from 35 to 40.6 per cent. The motility of the stomach was unaffected, the organ emptying itself identically in both instances, *i. e.*, in two and one-quarter hours (Fig. 10).

In a case of continuous hypersecretion a better effect was observed after the use of olive oil. One-half hour after the fractional test was begun 90 c.c. of olive oil were administered. The average total acidity was reduced from 101.5 to 81.6 per cent. on one occasion and from 94.5 to 87.6 per cent. on another occasion. The factor of hypersecretion was affected to a lesser degree.

ADMINISTRATION OF ALKALIES IN DIVIDED DOSES DURING DIGESTION. The previous observations of the effects of the alkaline earths on the gastric acidity demonstrated two phases of activity,

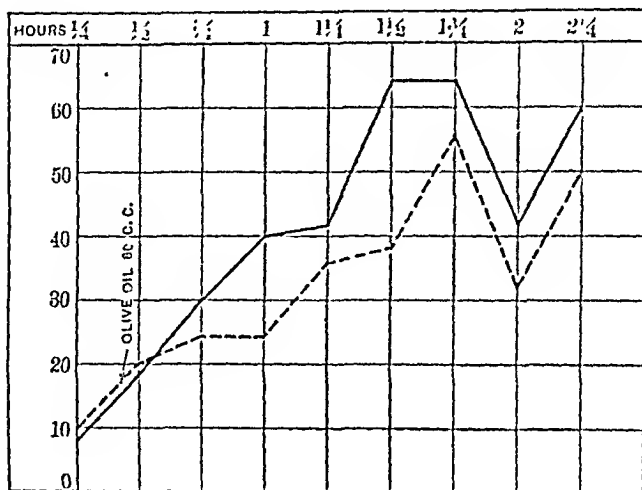


FIG. 10

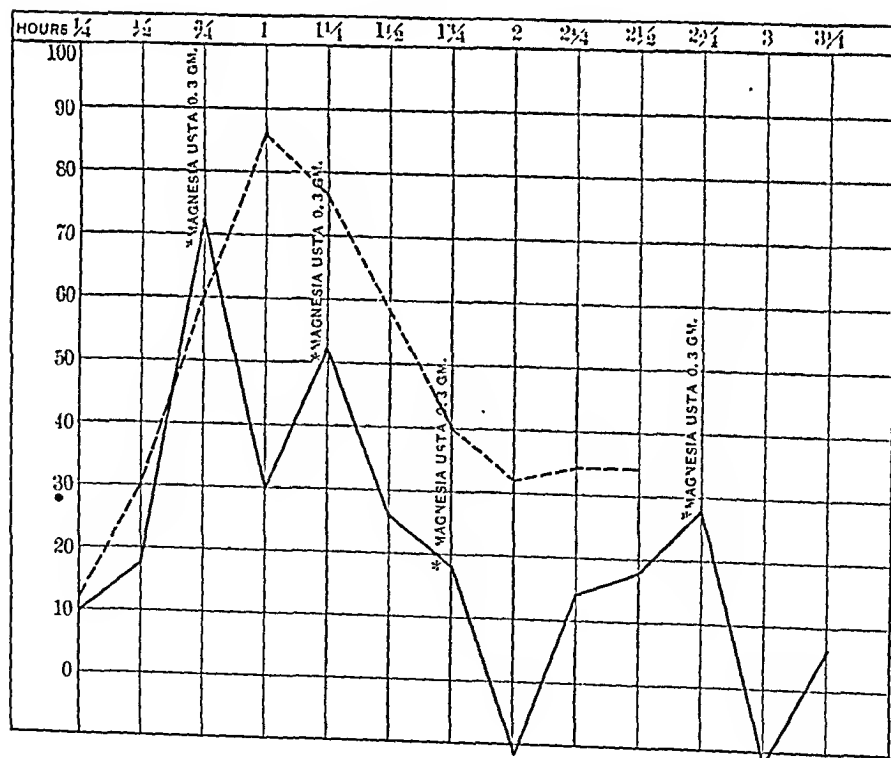


FIG. 11

a primary neutralization phase and a secondary or compensatory reaction marked by excessive acid production. The attempt was made to cause a continuous depression of the acid curve by dividing the single dose of alkali into aliquot portions and distributing these



portions over the course of the digestion. Calcined magnesia was chosen as the alkali to be tested, since the nature of its therapeutic activity had been previously ascertained. Thus after a single dose of magnesia (20 grains) it had been learned that the primary or depressant stage lasted about thirty minutes and was followed rapidly by a sharp rise in the acidity. A fractional dose of the magnesia (5 grains) was therefore administered every half-hour for four doses. The effect is charted in Fig. 11. A successful depression of the acid curve was accomplished, the neutralization of the acidity being both complete and permanent. In fact, the successive doses had an apparently cumulative action, so that after the third dose an alkaline reaction in the stomach contents was actually observed. The diminution of average total acidity was from 43 to 22.4 per cent.

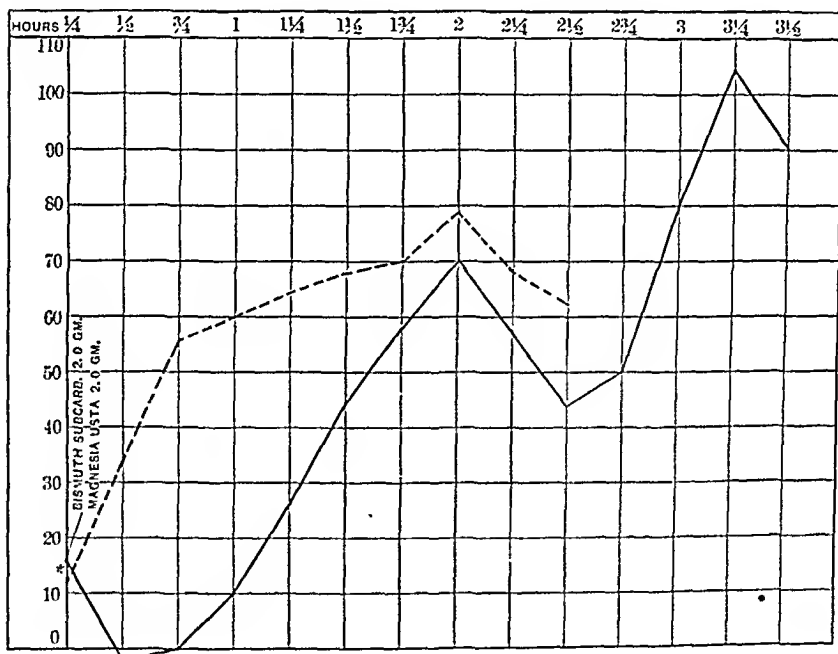


FIG. 12

**EFFECT OF ADMINISTRATION OF COMPOUND MEDICATION.** The therapeutic action of antacid agents in combination, was investigated by the administration of a compound powder after the ingestion of the test meal. The first combination investigated was: *R*—*Magnesiæ ustræ*, gr. xxx; *bismuth. subcarbon.*, gr. xxx. The resulting curve showed the predominance of the action of the magnesia. Following the taking of the powder there was a rapid neutralization of acidity to minus 4 per cent. (4 per cent. alkalinity), followed by a progressive rise to 104 per cent. total acidity. Free

acid was completely absent for one hour; motility was delayed to three and three-quarter hours (control time two and one-half hours). The average total acidity was unappreciably reduced from 56.8 to 48.8 per cent. The curve was divided into two phases: In the first an exaggerated and unphysiological depression took place and in the second just as unphysiological an hyperacidity was created. The magnesia effect was the predominant one, the deliberate and steady antacid qualities of the bismuth being unobservable. It was evident that the dose of magnesia had been too large.

A second combination powder of the following composition was administered:  $\mathcal{R}$ —Magnesiæ ustæ, gr. xv; bismuth. subcarbon., gr. xv; sodii bicarbon., gr. xx; atropinæ, gr.  $\frac{1}{100}$ .

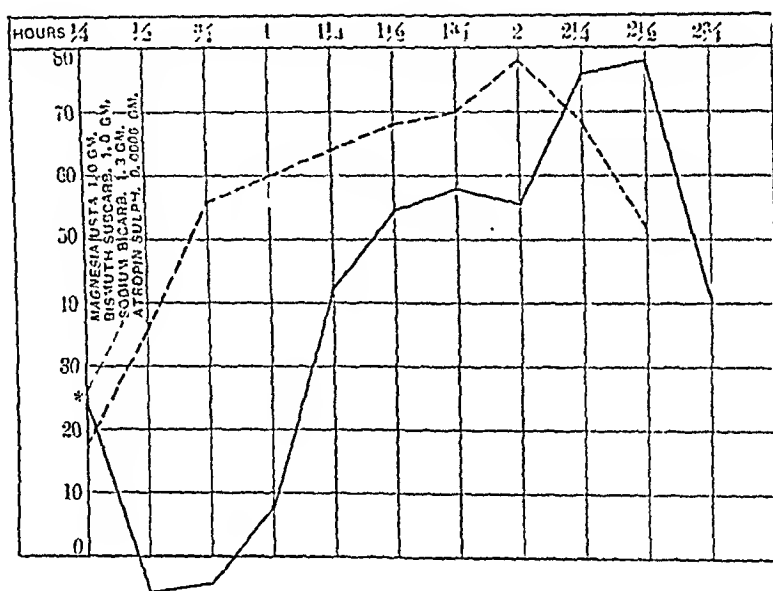


FIG. 13

A more moderate effect was here observed (see Fig. 13). The initial depression was too rapid and was carried too far because of the presence of the bicarbonate of soda; however, the secondary rise of acidity was also less marked because of the smaller dose of magnesia employed. The depression of average total acidity was from 58.6 to 38.7 per cent.; motility was not delayed. The late and more even action of the bismuth was more in evidence in this test.

As an example of the vicious use of an overdose of antacid agents the action of the following combination powder is cited:  $\mathcal{R}$ —Magnesiæ ustæ, gr. xxx; bismuth. subcarbon., gr. xxx; sodii bicarbon., gr. xxx.

An excessive, early and prolonged neutralization of the acidity was observed. An actual alkalinity of 70 per cent. occurred within fifteen minutes after the administration of the powder.

Free acid was absent for two hours, following which there was a return of the total acidity to 68 per cent. The diminution of the average total acidity was very marked, namely, from 58.8 to 13 per cent. It is self-evident that such an extreme depression was contrary to the physiological conditions for digestive activity, and was probably as deleterious, if often repeated, as the uninterrupted hyperchlorhydria would have been.

**DISCUSSION OF RESULTS.** The preceding experiments portrayed in an exact and concrete manner the method of action of the various agents commonly employed by the medical profession to encompass a diminution of the acidity of the stomach and of its secretion. The customary alkalies, sodium carbonate and calcined magnesia, were carefully studied, as were also bismuth subcarbonate, olive oil and atropin; the latter are constantly being empirically used for the attempted accomplishment of the same aim.

As regards the alkaline salts, both the soda and the magnesia act therapeutically in a relatively similar manner. Both neutralize the acidity at the moment of administration, the bicarbonate more quickly but less thoroughly, the magnesia more slowly but more effectively. The administration of either salt is followed by an irritative reaction in which the acid mounts quickly, to at least the level of the control test at the corresponding time. In most instances, particularly with the magnesia, the secondary rise in acid exceeds all previous levels. While it was true that the average total acidity may have been depressed when a sufficiently large dose was employed, yet this figure for acid diminution should be accepted with reserve, for it often gives a fallacious impression. Thus an immediate depression of acidity to minus 70 per cent. (70 per cent. alkalinity) may be counter-balanced by a secondary rise of acid titer to plus 110 per cent.; in such an instance the general average may be well within the normal figure and evidence no variation from the control average acidity. It now becomes apparent why such divergent results were obtained by Bourget,<sup>11</sup> Hayem,<sup>19</sup> Du Mesnil,<sup>8</sup> Lenoissier and Lemoine<sup>10</sup> and others, for each investigator chose a different time after the administration of the alkali at which to extract his test meal.

The interpretation of the charts of fractional estimations, throws a most illuminating light upon the mode of action of these salts as commonly employed. The custom of administering alkalies before meals, as is practised by some of the medical profession, is a mistake, for the reason that the meal comes at the time of the secondary reaction to the alkali and thus the digestive acidity is reinforced rather than diminished. The administration of these salts after the meal was attended by better results when the proper dose was chosen. Thirty grains of bicarbonate of soda produced no depres-

<sup>11</sup> Hayem: *Lecons de Therapeutique, les Agents Physique et naturels*, p. 609.

sion, in fact produced a rise in average total acidity, and yet the temporary neutralization was moderate and physiological and the secondary rise not exorbitant. Sixty grains caused a general depression, yet by generating a secondary medicinal hyperacidity defeated its own purpose. All in all the former dose was preferable at least for a case of moderate hyperacidity; a hyperchlorhydria which reaches 90 per cent. and over probably requires a proportionate increase in dosage.

The disadvantages of a large dose of magnesia, 15 grains or more, are: (1) That the initial depression is excessive, robbing the stomach of its essential free acid for a period varying from half an hour to two hours; during this period proteolysis is paralyzed, since free acid is essential to the digestion of proteid. (2) The subsequent reaction on the part of the acid-secreting cells is so vigorous that the therapeutic purpose is defeated. The dose of magnesia should therefore be a moderate one, 8 to 15 grains, depending on the degree of hyperchlorhydria one wishes to effect. Doses in excess of this tend only to emphasize the disadvantages incident to the use of the drug. It should never be forgotten that the neutralizing power of the magnesia radical is three and a half to four times as strong as that of the soda radical. The same rules that apply to magnesium oxide apply in general to magnesium carbonate, ammoniomagnesium phosphate, the soluble magnesium hydrate, and other magnesium preparations.

The exhibition of magnesium salts at the end of digestion effectually diminishes acidity and has a prolonged action.

The method of administering fractional doses of magnesia at intervals during digestion has proved to be the most practical manner of employing such a salt for the correction of hyperchlorhydria. Five grains of magnesia every half-hour is an excellent antacid for this purpose. The success of the fractional method of administering alkalies confirms the opinion of Bourget,<sup>11</sup> who suggested a saline-alkaline mixture to be sipped at frequent intervals after a meal. He proposed the following formula:  $\mathcal{R}$ —Sodii bicarb. puriss, 8; sodii phosphatis sic, 4; sodii sulphatis sic, 2. Misce fiat pulv. dent. tal. dos. Nr. x. Sig.—One powder dissolved in 1 liter of cold water.

The action of bismuth as an antacid is a highly satisfactory one. The neutralization of the acid is deliberate, moderate and prolonged, and a secondary rise of acidity is avoided. Bismuth subcarbonate has only 36 per cent. of the neutralizing power of an equal quantity by weight of sodium bicarbonate. The breaking down of bismuth subcarbonate to bismuth oxychloride takes place slowly, and it is probably because of the slow decomposition that a secondary acid reaction is prevented.

The action of olive oil was disappointing in that it rarely diminished the acid titer of the gastric contents. Good results were

seen only in cases of pure hypersecretion. The same disappointment applies to atropin given by mouth even in a single dose or in successive doses during the day. On the other hand, the efficacy of atropin administered hypodermically in cases of hypersecretion accompanying hyperacidity was quite evident. In these cases the acidity was diminished, and in addition the secretion of the gastric tubules was markedly inhibited.

The combination of a more slowly acting antacid, such as bismuth, with the more rapid and vigorous salts of magnesia or soda, is justified by the foregoing experiments. The antacid effect of the bismuth was observable throughout the secondary hyperacid stage produced by the more readily dissociable elements. As regards dosage, the same rules apply to drugs in combination as when they are singly administered. The dose should be a moderate one in both instances.

It becomes apparent from a closer study of these charts that a delay in gastric motility occurs as part of the action of the antacid salts. When moderate doses were used a partial neutralization of the free acidity tended to "slow down" the rate of activity of the gastric ferments. When larger doses were used paralysis of the proteolytic ferment (pepsin) was brought about and proteid digestion temporarily ceased. This, in itself, is a plausible explanation of the delay of motility. Basing one's judgment on the theory of the acid control of the pylorus as propounded by Cannon, one would be led to believe that the diminution of acidity would encourage a patulous pylorus and a more rapid emptying time. But the secondary rise in acid acts in a contrary manner to control and to delay this premature evacuation; the rising acidity toward the end of digestion in place of the customary declining acid values naturally tends to inhibit the emptying of the viscus. However, the delay was rarely prolonged and did not become at any time a considerable factor.

The natural secretion of mucus in the stomach is not apparently affected by the administration of the antacid medicaments.

The regurgitation of bile and duodenal juice, an occurrence which normally takes place in a large proportion of cases, varies only in a manner to parallel the fluctuations in acidity. This regurgitation is not a constant factor and may take place coincidently with a high acidity as well as with a moderate subacidity. The favorite time for the reflux flow of duodenal contents is toward the latter half of digestion, that is, during the period of declining acidity. After the administration of magnesia or bicarbonate, the secondary rise of acid may check this regurgitation of intestinal fluid. Whether this has at the present time any importance or significance, it is impossible to state.

**CONCLUSIONS.** In general one must feel surprise and disappointment upon realizing the mode of action of the antacid agents, more

particularly the alkaline salts. It is immediately obvious that much misuse of these therapeutic potentialities has taken place in my experience, as well as in the hands of others. With too small a dose no beneficent neutralization is accomplished, while the attendant secondary rise in acidity rarely fails to assert itself. When too large a dose is employed one risks paralyzing the digestion for a considerable period, following which there appears a hyperacidity of even greater degree than the one we undertook to combat. The combination of slowly acting, with more rapid alkalies, is desirable. Atropin has a restricted use and should be employed only as a desiccating agent in instances of hypersecretion.

The use of fractional doses of the alkalies distributed over the course of digestion is the most efficient and physiological method for the employment of these agencies; for this purpose magnesium oxide is the most dependable and best suited salt.

Based upon these studies it seems very questionable whether prolonged use of the alkalies leads to any permanent diminution of the acid secretion of the stomach; in fact, it is as likely that the opposite effect is produced.

A lasting relief of hyperacidity is not to be sought in antacid medication, nor in olive oil or atropin. It is more likely to be found in the proper regulation and restriction of dietary errors as well as in the general control of the hygiene and manner of living of each individual patient under our professional care.

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## RELAPSING FEVER ENDEMIC IN COLORADO.\*

BY JAMES J. WARING, M.D.,  
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WHEN peace is declared the returning flood tide of Americans whom the business of war has called to foreign shores will bring with it necessarily the menace of new diseases now rare or perhaps unknown in the United States. At this time, when the wave of humanity is still moving toward the other side, it is desired to report a case of relapsing fever, a disease all too common in Europe but exceedingly rare in this country.

The following case is important not only for its own sake, because of its rarity, but because the infection was contracted undoubtedly in the same locality as Meader's cases, reported two years ago.

At the Annual Meeting of the Colorado State Medical Society, October 5, 1915 Meader<sup>1</sup> presented clinical histories of 5 cases of relapsing fever, in 2 of which he had found the spirochete. This

\* Read before the Medical Society, City and County of Denver, October 13, 1917.

most valuable observation represented the first report of this disease in Colorado. Neither before nor since have any other cases been recorded in this State. Indeed it is many years since relapsing fever has been proved beyond question in American residents of the United States, although it has been found in a few instances among recently arrived immigrants.

Todd<sup>2</sup> says the disease is not endemic in North America. Osler<sup>3</sup> mentions its occurrence in epidemic form in New York and Philadelphia in 1869, adding—"since when it has not reappeared."

Carlisle<sup>4</sup> in reporting 2 cases of relapsing fever in May, 1906, writes—"there are no other cases on record in this country up to the present time in which *Sp. obermeieri* has been found in the blood." The origin of one of his cases (an Englishman and ship steward) was undoubtedly tropical America. The other was a case of accidental infection of a laboratory worker (the joint author of a paper<sup>5</sup> on this subject in the same journal) from an inoculated monkey. The geographical data incorporated in this paper of Carlisle are most complete.

Clymer<sup>6</sup> credits the Irish immigrants with bringing the disease to Philadelphia in 1844, all of the 15 cases under his care crossing the ocean in the same vessel. A. Dubois<sup>7</sup> reported a study of 15 cases in 1848. Austin Flint<sup>8</sup> published a lecture in 1870 based on his experiences with the disease in the wards of Bellevue Hospital. To his article was appended a statistical report of 103 cases by T. J. Moore.<sup>9</sup>

The disease appeared in epidemic form in New York in 1869 and continued throughout the year and the next, gradually disappearing in 1871. This outbreak was confined chiefly to Philadelphia and New York, although a few cases were found in Washington, in Maryland, in New Jersey and in Connecticut. One case was imported into Boston as noted in the American translation of Strümpell's work on the *Practice of Medicine*.<sup>10</sup>

In September, 1874, a severe epidemic<sup>11</sup> was observed at Oroville, California, among chinese laborers. This epidemic resembled both *typhus exanthematicus*, or ordinary typhus fever, and *typhus recurrens*, or relapsing fever. It was probably the latter, but there is no conclusive evidence, as Obermeier<sup>12</sup> did not publish his observations until 1873, although he found spirochetes in the blood of a patient in 1868.

Ward<sup>13</sup> reports a case in an Armenian in Worcester, Mass., in 1899. However suggestive clinically, the diagnosis was not confirmed by the blood examination.

It will then be noted that until Meader's cases were placed on record there were no instances that I have been able to find of this disease with the spirochete demonstrated in the blood originating in the United States among native Americans.

Meader concluded his paper in 1915 as follows: "These cases are

reported for the purpose of calling attention to the existence of this disease in Colorado so that the members of this Society may be

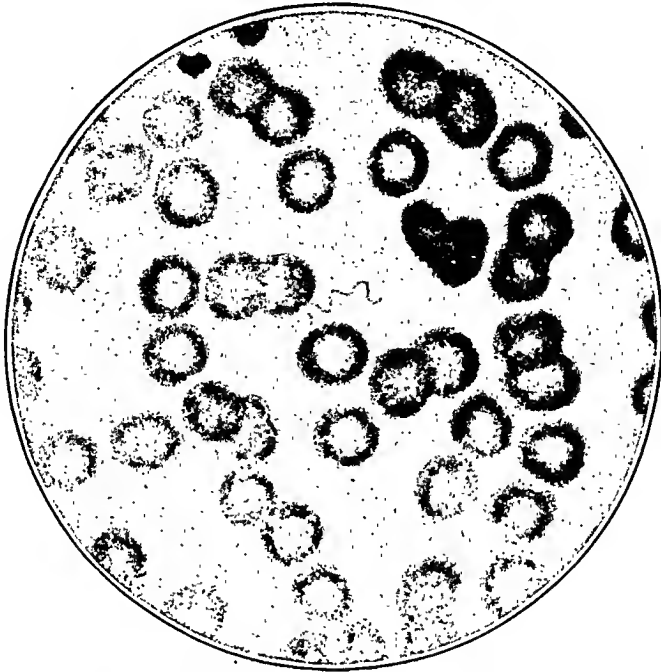


FIG. 1.—Spirochete in the blood. (Mender's case.)

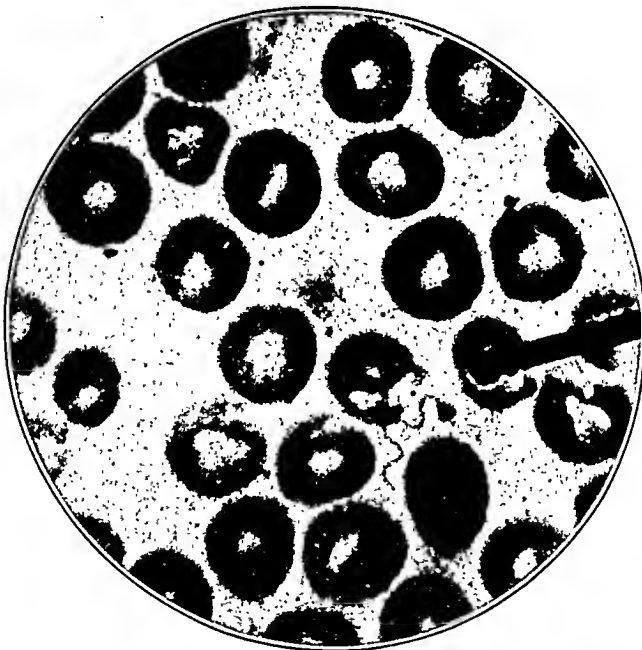


FIG. 2.—Spirochete in the blood. (Waring's case.)

especially on the watch for it to determine if this be only a sporadic accidental outbreak or if we have an endemic focus."



The case whose clinical history follows is placed on record as proving beyond doubt the presence of such an endemic focus in or near Bear Creek Cañon, Colorado.

The patient, a native American, was a boy, aged twelve years. His father has been ill for the past three years with pulmonary tuberculosis and is now an arrested case. The boy himself was examined two years ago by A. C. Foster and G. B. Gilbert, of Colorado Springs, and by them considered to have a slight glandular and pulmonary infection. While under my care this past winter he showed definite evidences of tuberculosis. He came to Colorado July, 1915, and has not been out of the State since except from October 1, 1916, to October 25, 1916, when visiting in Kansas City. He resided in Colorado Springs continuously from his arrival, and saving only for this above-mentioned visit, until he came to Denver, March 12, 1917. July 6 to July 9 he spent at Lake Wellington near Buffalo Park. From August 1 to August 7 he was at Troutdale, Bear Creek Cañon, returning to Denver on the latter date and was taken sick August 12. As the incubation period rarely exceeds eight days the infection must have been contracted at Troutdale.

On Sunday, August 12, the boy was drowsy and disinclined to play. On August 13, he had a chill in the early morning and temperature rapidly rose to  $104^{\circ}$ . On August 14 it went to  $105.2^{\circ}$ . By August 16 it had returned to normal. I saw him first on August 13. He was torpid, skin very sallow—almost icteric, eyes bright, cheeks flushed, a herpetic eruption on his upper lip, tongue coated, breath heavy, and complaining bitterly of headache and pains through the back and legs. He also had pain and tenderness over the spleen which was markedly enlarged. The liver was not notably increased in size, nor were heart and lung findings different from former examinations. Bowels were constipated, he had vomited twice and did so repeatedly during this attack and subsequent paroxysms. I might note here that the spleen was palpable throughout his illness but increased considerably in size during the paroxysms, becoming smaller but still palpable in the intervals.

#### WHITE BLOOD COUNTS.

	8/14	8/24	8/31	9/4	9/10
White cells . . . . .	6400	7200	9000	8200	12,900
Polymorphonuclears . . . . .	..	57	62	58	69
Large lymphocytes . . . . .	..	15	13	2	7
Small lymphocytes . . . . .	..	11	18	40	23
Transitionals . . . . .	..	15	7	0	1
Eosinophiles . . . . .	..	2	0	0	0
Basophiles . . . . .	..	0	0	0	0
Absolute lymphocyte count . . .	..	1872	2790	3280	3870

In spite of the acute onset typhoid fever was considered a possibility, this suspicion being warranted more or less on the grounds of an enlarged spleen and a leukopenia. The Widal test and blood

culture were both negative and as these reports came in from the laboratory the first crisis occurred, the temperature falling rapidly with moderate sweating to normal. With the subsidence of fever, appetite returned and the malaise disappeared as if by magic. I confess to being puzzled by the return of fever on August 20. On this day he had a hard session with the dentist in the morning, with gradually rising fever in the afternoon. The lung findings were as before except for the presence of deep-seated, distant, subcrepitant rales scattered over the right back and heard only after cough. In this connection Hagler<sup>14</sup> writes that fine moist rales were found in the chest frequently throughout the first few days of the febrile period. There was no cyanosis, pulse 120, eyes and reflexes normal. The spirochetes—probably *Spirochaeta novyi* were found by my associate in the laboratory, Dr. Ward Burdick, searching at my suggestion, during the second attack. They were overlooked at the first paroxysm but found in these slides on careful subsequent examination.

There was an absence of the urinary findings noted by Meader. I refer to the appearance and disappearance with the paroxysms of a considerable amount of albumin and large numbers of fine hyaline casts. Albumin was found only during the fourth paroxysm.

The differential and total white blood counts are tabulated. Meader calls attention to a rise in the transitionals during the attack and a slightly increased white count and fairly normal differential count during the interval, with corresponding inverse variations in the polymorphonuclear neutrophils. The counts in this case were made at irregular times in relation to the paroxysm so that deductions are difficult, but it would appear on careful study that Meader's findings are not altogether borne out. One fact is strikingly evident. There is a steady increase in the absolute lymphocyte count. In this connection it will be recalled that Novy and Knapp,<sup>15</sup> who with Gabritschewsky<sup>16</sup> contributed much to the study of immunity in this disease, consider the role of the mononuclear phagocytes most important in the ingestion of dead and enfeebled spirochetes under the influence of immune bodies.

The third paroxysm came on August 29, after three days of fever to as high as 99° with the crisis on August 31. There was then an interval of nine days with temperature to 99° or slightly over before the next paroxysm. That the boy was not well during the second and third intervals was evident from the fact that his spleen was still palpable and that he had an occasional elevation of temperature to 99° or slightly over.

Seven days after the third attack there began a mild febrile movement, the high daily point being from 99° to 99.5°. The crisis with fever to 104° plus came on September 9, with normal temperature again on September 11. Exactly seven days after the subsidence of this attack, or on September 17, the temperature was 98.1° at

7 A.M.; at noon it was 99.5°; by 4.30 P.M. it had risen to 110.8° and by 10 P.M. was just short of 105°. Four hours later, or at 2 A.M., of September 18, the temperature was 98.2° and it has remained within normal limits ever since. The patient, somewhat thin and weak after his illness but otherwise in excellent condition, was kept in bed until twelve days had elapsed without fever before permitting him to get up, it having been the general experience<sup>17</sup> that if this interval elapses without a paroxysm none is likely to occur.

DISCUSSION. As transmitting agents bed-bugs, head-lice, body-lice, ticks, fleas and biting flies have all been suspected. Flügge, in 1891, was probably the first to suggest the possibility that vermin might convey relapsing fever in Europe. "Only once have spirochetes been transmitted by the bites of bed-bugs" says Todd. He thinks this was not a true transmission by inoculation but the spirochetes were carried mechanically on the mouth parts of the bugs.

Cuthbert Christy,<sup>18</sup> in India, in 1902, allowed himself to be bitten without becoming infected by bed-bugs caught in the bed of a patient ill with relapsing fever.

Noguchi<sup>19</sup> in a recent exhaustive consideration of spirochetes says: "in the case of *Spironema recurrentis* both body-lice and bed-bugs may be infected by sucking the blood of a patient suffering from the European relapsing fever, but the lice alone can transmit the disease to the next person they bite. Bed-bugs are never known to spread the infection by their bites, although by crushing the infected bugs directly over a minute skin trauma (scratch, etc.), a person may become infected." Breinl and Kinghorn,<sup>20</sup> among others, failed in their attempt to transmit spirochetosis by bugs.

Hagler<sup>21</sup> is inclined to ascribe to the bed-bug a definite and more important role. From a large experience in Serbia he has the following observations to make: Typhus and relapsing fever appeared coincidentally in Serbia, and the same preventive measures were effective against both. Typhus fever practically disappeared as the lice were exterminated but relapsing fever persisted until fumigation of rooms and wards with sulphur was undertaken to destroy the bed-bugs, after this it disappeared. Of 50 Red Cross surgeons and nurses at least 20 contracted typhus while none developed relapsing fever. Typhus is admittedly conveyed by the louse and probably more nurses and doctors were bitten by lice than by bed-bugs. These latter have been shown to harbor the *Spironema recurrentis* for as long as sixty days<sup>22</sup> but as noted above, according to Noguehi and other investigators they do not transmit the disease.

The *Pediculus corporis* carries European relapsing fever, but even as close a relative as *Pediculus capitis* has been shown by Gonder<sup>23</sup> to be incapable of spreading the disease, although its body may contain the organisms.

Robledo<sup>24</sup> thinks *Argas americanus* is the tick responsible for the spreading of *Spironema noryi* in Columbia, but this needs confirmation.

Hagler says the tick in Serbia could be excluded as a vector because of its rarity.

In conversation with Dr. Meader I learned of certain ideas of Prof. Theo. D. A. Cockerell, of the University of Colorado, as regards the biting fly as a transmitting agent. The following facts I obtained through Prof. Cockerell. There occurs during the summer months in the mountains of Colorado a powerful biting fly, by name *Symphoromyia*. This fly is found also in the mountainous districts of Europe where relapsing fever occurs. The localities where certain genera are found are as follows:

*S. atripes*. Rabbit Ear Pass—Long's Peak Trail on way from Long's Peak Inn.

*S. hirta*. Marshall Pass, 10,856 feet. Long's Peak Trail, on way from Long's Peak Inn. Webber Ranch—between Ward and Allen's Park.

*S. pullata*. "Colorado."

*S. trivittata*. "Colorado."

Prof. Cockerell also sent me sketches of the wings of the buffalo gnat and the *symphoromyia*. It is highly improbable that these flies have anything to do with the transmission of this disease. I have been able to find little information on them as possible vectors. Nuttall<sup>25</sup> tried for a long time unavailingly in England to convey the *Trypanosoma brucei* by means of the genus of biting flies called *Stomoxys*. Schuberg and Kuhn,<sup>26</sup> however, record a successful transmission of relapsing fever by *Stomoxys*.

How did the disease enter Colorado? It is not only possible but perhaps probable that the band of gypsies mentioned by Meader, that stopped in Bear Creek Cañon at the tent where Meader's patients resided left behind certain undesirable visitors in the form of infested body-lice. Granted this, it follows that the descendants of these pediculi either retained infecting ability from the summer of 1915, until the summer of 1917, a very remote possibility, or other unrecognized causes have come and gone and the said descendants have had opportunity for receiving their infecting store of spirochetes. In any case it seems beyond doubt proved that an endemic form of relapsing fever has been established in Colorado.

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## A VACCINE FOR THE TREATMENT OF BRONCHIAL ASTHMA: REPORT OF TWENTY CASES.<sup>1</sup>

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AND

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THE work of Auer and Lewis, Meltzer, Vaughan, Babcock and others leaves little doubt that the disease so long known as bronchial or idiopathic asthma has been permanently removed etiologically from the neuroses, and is now fully explained as a manifestation of protein sensitization. The paroxysmal outbursts represent anaphylactic shock and the various causes formerly thought to act reflexly, and whose removal often resulted in cure, are now believed to be foci from which the foreign material necessary to induce an attack is elaborated.

Judging from the widely diversified nature of the exciting causes of asthmatic seizures it would seem probable that the specific poison either occurs in a number of forms or is common to a great variety of plants and animals as well as bacteria. Moreover, from our understanding of the conditions underlying sensitization it is evident that an immunity could be produced provided the specific protein was capable of being isolated in an available form and

<sup>1</sup> Read before the Nineteenth Annual Meeting of the Tri-State Medical Society, at Durham, N. C.

injected into the sensitized individual in suitable amounts and at proper intervals. This procedure, however, assuming that it was possible in more than a limited number of cases, would involve an amount of time and work far exceeding the means of the average sufferer from asthma.

Certain observations of the writers, derived from the study of a considerable number of cases of asthma, have strongly suggested the possibility of the presence of the specific protein in the bronchial secretions of the patient himself, and also that this protein may be recovered in suitable form for use in bringing about immunity.

In the fall of 1915 we began to prepare vaccines for asthma cases along the lines suggested by Babcock. From our first patient we succeeded in growing the organism described by him, along with a few streptococci and staphylococci. The result in this case was truly remarkable. The second or third injection was sufficient to give immediate and absolute relief for a period of a year. In our second attempt at sputum growth from an asthmatic we failed to grow Babcock's organism and despaired of making up the vaccine because of the fact we were led to believe from his results that his organism was specific for this condition. We did, however, prepare a vaccine from the growth which contained streptococcus, staphylococcus and *Micrococcus catarrhalis* along with a small amount of broth-culture media. The result in this case was even more striking than the first. Our third case was treated with the mixture of the broth sputum and the bacterial flora, and the outcome of the treatment was equally as startling. We then abandoned the anaërobic method of culture and commenced to grow our organisms by aërobic methods. More recently we have been adding a drop or two of guinea-pig serum along with the sputum and broth and incubating the whole for a period of forty-eight hours before making up our vaccine.

Our present vaccine is made in the following manner: 1 c.c. of washed sputum is incubated in 10 c.c. of broth and 1 or 2 drops of guinea-pig serum for a period of forty-eight hours. At the expiration of that time the culture is standardized and killed by heat of 60° C. for a period of two hours. Further decomposition is prevented by adding carbolic acid until a 1 per cent. solution results. This is cultured out to ensure sterility of our suspension. The vaccine is then diluted with normal saline until each cubic centimeter of the suspension contains 500,000,000 to 1,000,000,000 organisms. The initial dose is 5 minims and each subsequent dose is increased by 1 minim. We do not increase beyond 15 minims, although we may continue the treatment several weeks after this amount has been reached.

At first glance this mixture seems to be a gunshot one, but a more careful survey of its constituents and the results obtained by its administration should, in our opinion, warrant its use. It

is quite possible that the anaphylatoxin that is responsible for asthma may be produced *in vitro*, and that the proper administration of this anaphylatoxin may give a relative immunity to further intoxication.

Friedberger succeeded in producing toxic substances *in vitro*, and these gave rise to typical anaphylactic symptoms when injected into normal animals. In later experiments, however, he obtained similar poisons from bacteria and other proteins by their incubation with normal guinea-pig complement without the concurrence of a specific antibody; while other observers have been able to isolate similar poisons by the incubation of normal guinea-pig serum with starch, agar, etc., and have decided that the poison originated from the serum. Friedberger, however, objected to this on the grounds that the small amount of protein impurities in the agar and starch furnish the material for the formation of the anaphylatoxin.

The exact nature of asthma anaphylatoxin then is still unknown, but it is reasonable to believe that the anaphylactic symptoms are produced by the digestion and the split products of the sputum, bacteria, etc.

It has been observed that animals receiving injections of a foreign protein at short intervals develop a decided resistance to this substance, so that several lethal doses for a sensitized animal may be given without producing symptoms. If, however, the time between injections is sufficient to sensitize the animal anaphylactic shock will result. In other words, frequent doses at short intervals will confer an immunity to a protein, while if the dose is spaced over a period of eight to ten days the animal becomes hypersensitive. In giving vaccine we attempt to raise the resistance of our patients against the anaphylatoxin of asthma. In other words, we vaccinate against anaphylaxis, and the resulting state might be called anti-anaphylaxis.

We have been able so far to observe the effect of this plan of treatment in 20 cases of typical bronchial asthma.

In 12 of these cases complete relief from attacks was experienced after from one to five injections of the vaccine and this relief has persisted up to the present time. The longest period of freedom from symptoms is sixteen months, the shortest six weeks.

In 5 cases distinct improvement has been noted either in the frequency of the seizures, their severity, or their duration. In 3 of these cases improvement occurred only after a second vaccine had been made and administered at shorter intervals than the first.

In 2 cases no effect at all was produced. One of these patients was an elderly man with emphysematous lungs and a history of asthma extending over twenty years. Asthma in the other case had followed injury to the chest and roentgen-ray examination revealed ununited fractures of several ribs.

In 1 case administration of the vaccine seemed to increase the

intensity of the paroxysms, a result which appeared to be explained by the fact that too long a time was allowed to elapse between injections.

Injections have in most cases been made twice a week. We are of the opinion, however, that a shorter interval will prove more desirable. We have also attempted, in each case, to remove an obvious focus of infection, but have refrained from any other treatment while the vaccine was being used.

We have been greatly impressed by the above results and hope to determine in the near future (1) whether or not the elements constituting the mixture are effective if injected separately; (2) also which element is potent; (3) and whether the protein injected is specific or not.

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## A STUDY OF ATMOSPHERIC AIR IN THE UPPER DIGESTIVE TRACT.\*

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It is only within recent years that sufficient attention has been accorded to the role played by atmospheric air in the physiology and pathology of the digestive tract. Although the symptoms associated with the presence of gas—belching, tympany, meteorism, flatulence, etc.—have been the subject of comment from the earliest times, it has most commonly been taken for granted that the gases in question have had their origin entirely within the body, whether from the decomposition of food, the exhalation of vapors or from the interplay of gas-producing juices. It would seem therefore advisable, before presenting any observations based on newer methods, to pass in brief review the more important of the many scattered observations of earlier writers.

### I. HISTORICAL BACKGROUND.

Interest in the subject dates back to the time of Hippocrates, to whom is ascribed a book on the "winds" or "flatuosities."<sup>21</sup> Following this authority, many of the ancients created an entity of the condition, to which they gave the name *morbus ructuosus*, and ascribed all sorts of disorders to it. These men became known as "pneumatists." This doctrine was energetically opposed by Combalusier (1747),<sup>11</sup> who attempted to give a more restricted significance to the role played by the gases.

\* Read in part under the title of "The Physiology of Acrophagia," at a meeting of the Section on Medicine of the New York Academy of Medicine, December 18, 1917. Dr. Meltzer discussed the paper and his remarks are published in the Medical Record, 1918, xciii, 100.



Although as far back as 1652 a study of the intestinal gases had been made by Van Helmont,<sup>19</sup> it was not until the end of the eighteenth century that the indefinite notion of *morbus* was abandoned and that interest was centered on the actual composition and origin of the gases (Jurine (1789),<sup>25</sup> Gerardin (1814),<sup>17</sup> Magendie and Chevreul (1814),<sup>32</sup> Vauquelin (1817),<sup>51</sup> Lameyran and Fremy (1819),<sup>29</sup> etc.). As material, both humans and animals were used. The human subjects were examined apparently only postmortem, freshly executed criminals being common objects of study. Despite the presumably crude methods employed, the basis for the chemistry of the subject was really laid down in these investigations.

At this period also we have the first clear account of air-swallowing in Magendie's report of the case of a conscript who practised auto-inflation in order to avoid military service (1813).<sup>76</sup> In 1832 Baumès<sup>4</sup> published a series of letters in which he strongly advocated the view that under appropriate irritation the mucous membranes could give rise to a gaseous flux, just as they do to a mucous or serous or hemorrhagic flux—*ubi stimulus, ibi fluxus*. This work is the historic basis for the theory of "alimentary respiration."

With the exception of the careful quantitative studies of Chevillot (1833)<sup>8</sup> on the gases of man in health and disease, not much of importance was added by French scholars until the renewed interest in air-swallowing late in the nineteenth century. On the other hand, German workers began to contribute extensively to our knowledge of the gases of fermentation. Apparently their interest was first directed in this channel by the discovery that inflammable gases may be present in gastric contents\* and a rather rich literature was created on this subject alone (Carius (1865),<sup>7</sup> Popoff (1870),<sup>42 43</sup> Emminghaus (1872),<sup>14</sup> Ewald (1874),<sup>15</sup> Schultze (1874),<sup>47</sup> Hcynsius (1874),<sup>20</sup> Poensgen (1879),<sup>41</sup> Korach (1880)<sup>23</sup>). These investigations were expanded until the whole question of gastric fermentation and putrefaction was covered, not only from its chemical aspect, but from the bacteriological and general clinical view-points as well (Naunyn (1882),<sup>39</sup> Miller (1885, 1886),<sup>34 35</sup> Minkowski (1885),<sup>37</sup> Riegel (1892),<sup>44</sup> Kuhn (1892),<sup>27 28</sup> Hoppe-Seyler (1892),<sup>22</sup> Boas (1892),<sup>6</sup> McNaught (1893),<sup>33</sup> Straus (1894, 1896),<sup>45 49</sup> Dallemagne (1895),<sup>12</sup> Mills (1896),<sup>36</sup> Basch (1908)<sup>3</sup>).

Interesting as this work is, it should be noted that in the last analysis it throws light on but a single pathological condition, namely, pyloric obstruction with gastric fermentation and putrefaction, and that it gives but indirect evidence, if indeed any, as to the ordinary sources and behavior of the gastric gases. Of really greater importance for this purpose are the experimental contributions of Planer (1860),<sup>40</sup> Tappeiner (1882),<sup>50</sup> Schierbeek (1892, 1895),<sup>45 46</sup> Giglio

\* "Als (Patient) beim Anstecken einer Cigarre zufällig aufstossen musste, zum ersten Mal zu seiner nicht geringen Verwunderung die Brennbarkeit seines Ructus constatirte, und immer wieder . . . demonstrieren konnte." Ewald.<sup>15</sup>

(1905),<sup>18</sup> Woodyatt and Graham (1912),<sup>53</sup> and Yllpö (1916).<sup>54 55</sup> The general trend of most of this work is toward the belief that the basis of gastric gases under normal conditions is constituted by atmospheric air, modified in its composition by certain definite processes to be described later in this paper.

Mention has already been made of the work of Magendie. This illustrious physiologist pointed out that air-swallowing was akin to the "cribbing" of horses, that the condition was by no means a rare one—he found it in at least eight out of one hundred students examined—and that it could be acquired by practice. He also made the first attempt at describing the mechanism of the act itself. Despite the publication in the succeeding years of several special articles on the subject (Pierquin (1830),<sup>82</sup> Heusinger (1862),<sup>67</sup> Falke (1863),<sup>65</sup> Piorry (1871),<sup>83</sup> Weissgerber (1878)<sup>91</sup>), as well as the mention of air-swallowing as a possibility in some of the general medical works of the period (*e. g.*, Chomel (1842),<sup>9 10</sup> Andral (1848),<sup>1</sup> Luton (1870),<sup>30 31</sup> Eichhorst (1887)<sup>13</sup>), it was never fully realized that air-swallowing is a perfectly normal physiological process, nor that under pathological conditions it may give rise to disturbances generally assumed to be due to gases originating within the body.

Indeed, it was not until the publication, in 1889, by Quincke<sup>85</sup> and in 1891 by Bouveret<sup>58</sup> that the present view-point was given complete expression. Bouveret's term "aërophagia" was immediately accepted and confirmatory papers followed each other quickly (Rosenbach (1889),<sup>86</sup> Aubert (1891),<sup>57</sup> Pitres (1895),<sup>84</sup> Obici (1895),<sup>80</sup> Vauthey (1896),<sup>52</sup> Vincens (1900),<sup>93</sup> Lioussier (1901),<sup>73</sup> Lyonnet and Vincens (1901),<sup>75</sup> Mathieu and Follet (1901),<sup>77</sup> Soupault (1901),<sup>89</sup> Bouveret (1901),<sup>59</sup> Perrody (1902),<sup>81</sup> Morange (1903),<sup>79</sup> Mathieu (1904),<sup>78</sup> Spivak (1905),<sup>88</sup> Dobrovici (1906),<sup>62</sup> Ewald (1910),<sup>16</sup> Thomas (1912),<sup>91</sup> Leven (1913),<sup>71</sup> Bucholz (1913)<sup>60</sup>). Roentgen-ray observations have been reported by Abrams (1898),<sup>56</sup> Variot (1901),<sup>92</sup> Hoffmann (1905),<sup>68</sup> Soupault (1906),<sup>90</sup> Lesage, Leven and Barret (1908),<sup>70</sup> Leven and Barret (1909),<sup>72</sup> Thomas (1912),<sup>91</sup> Eisler and Kreutzfuchs (1912),<sup>64</sup> Kraus (1912, 1913),<sup>107 108</sup> Barelay (1913),<sup>57 bis</sup> Leven (1913),<sup>71</sup> Smith and LeWald (1915).<sup>87</sup>

## II. THE NATURE AND ORIGIN OF THE GASES ORDINARILY PRESENT IN THE STOMACH.

Although it is perhaps now generally recognized that air is constantly being swallowed by normal individuals, it is not so widely admitted that the gases of the stomach are derived entirely from the atmosphere. Clinicians have long puzzled over the nature of certain violent outbursts, in patients proved to be free from gastric fermentation, of acute meteorism, generally associated with eructations of apparently enormous quantities of gas. Some writers have attempted

to include all such cases under the head of aërophagia, and Buchholz<sup>60</sup> has devoted a thesis to the proof that even the most severe forms (acute gastric dilatation) are nothing but aërophagia in riot. Others have from time to time advanced the hypothesis that there is sudden nervous relaxation of the pylorus with regurgitation of (preformed) intestinal gases or of alkaline duodenal contents (Benedict<sup>5</sup>) into an acid stomach with a consequent liberation of carbon dioxide. To be sure, Hoppe-Seyler<sup>22</sup> did find increased amounts of  $\text{CO}_2$  in the stomach in the presence of duodenal regurgitation, and the explanation as advanced cannot be denied *ex cathedra*. However, the experimental evidence thus far available seems

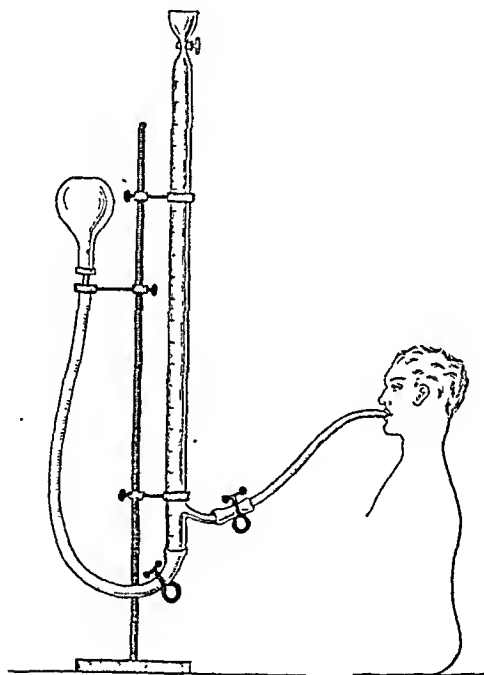


FIG. A.—Hoppe-Seyler's apparatus for analyzing the gas of the stomach.

opposed to this view, for Schierbeek<sup>45</sup> found that the gas values obtained in the stomach under various conditions were the same whether the pylorus was artificially closed off or not, and Dobrovici<sup>62</sup> showed that the pressure in the small intestine can be increased without regurgitation until, at 40 cm. of water, it is the ileocecal valve and not the pylorus that gives way under the strain.

On the other hand, a third theory, already mentioned under the name of "gastric or alimentary respiration," deserves more detailed consideration. If the gaseous constituents of a normal stomach are removed and analyzed, generally nothing but oxygen, nitrogen, and carbon dioxide will be found in proportions approximating, but

never quite the same as, those of atmospheric air. This investigation may be carried out in several ways. Perhaps the simplest, though possibly the crudest manner, is to collect the gas of eructations directly, as was done by Ewald and Rupstein<sup>15</sup> in their case of pyloric obstruction. Another method is to introduce a tube and obtain the entire contents of the stomach (Hoppe-Seyler,<sup>23</sup> Yllpö<sup>64</sup>). In animals more elaborate procedures can be carried out. Thus Schierbeck, in his classic studies of CO<sub>2</sub> tension,<sup>45</sup> <sup>43</sup> filled the stomach with water, withdrew the fluid after an interval sufficient for complete absorption and estimated the CO<sub>2</sub> after driving it off by boiling into a standard baryta solution. Woodyatt and Graham,<sup>53</sup> in their confirmatory investigations, preferred to fill the stomach with air and to estimate the CO<sub>2</sub> carefully in the resultant gas mixture. Giglio<sup>18</sup> punctured the stomach directly and thus obtained gases absolutely free from secondary air contamination.

In a few preliminary estimations\* undertaken on an unselected series of individuals aspirated at various intervals after eating, I obtained the following values:

Specimen.	Gas recovered, c.c.	CO <sub>2</sub> per cent.	O per cent.	N per cent.
1	49.5	4.4	19.1	76.5
2	12.2	4.1	13.6	82.3
3	36.9	0.2	18.5	75.3
4	48.2	2.0	17.0	81.0
5	43.4	4.1	17.2	79.0
Average	39.6	4.16	17.08	78.82
Inspired air (after Howell)		0.04	20.96	79.0
Expired air (after Howell)		4.38	16.02	79.0

These figures confirm those originally reported by Hoppe-Seyler<sup>22</sup> on the aspirated gases of non-obstructed cases as well as those reported by Pitres,<sup>81</sup> by Soupault<sup>89</sup> and by Linossier<sup>72</sup> on the gases of eructations.

The striking feature in all these results is the relatively high pro-

\* The apparatus employed was the simpler one of the two devised by Hoppe-Seyler,<sup>23</sup> the stomach contents being obtained by aspiration with an Ewald bulb, instead of by siphonage with a funnel as originally recommended (see Fig. A). The outfit consists essentially of a graduated tube (in which the gases are collected and analyzed) provided with two wide outlets at the bottom, and a narrow one at the top. The uppermost opening, closed off by a stop-cock, is connected with a thistle funnel through which the necessary reagents are admitted. The upper of the two lower apertures is connected with the stomach-tube (single opening at the end) and the lowermost of the two with the aspirator. Both can be closed off with pinch-cocks. The entire apparatus, including the stomach-tube, is filled with water, the end of the tube being sealed off with a plug of vaseline, and the exhausted aspirator is attached to the distal end of the system. The tube is then introduced into the stomach, and aspiration commenced. The gas volume may be read off directly from the graduations. The CO<sub>2</sub> is absorbed in 20 per cent. KOH, the oxygen in strongly alkalized pyrogallol solution. The nitrogen is estimated by difference. These experiments were performed in the summer of 1916 in the Laboratory of the Department of Physiology of Columbia University. It is a pleasure to acknowledge the kind interest of Professor Lee and his generosity in providing the necessary apparatus.

portion of carbon dioxide. This gas obviously cannot come from admixture with expired air, for it occurs in amounts equal to if not greater than the latter. What, then, is its origin?

As early as 1814 Gerardin and Magendie<sup>17</sup> tied off loops of intestine in dogs and found an accumulation of gas which they attributed to vital secretion of the mucosa. As already mentioned this theory was elaborated particularly by Baumès in 1832.<sup>4</sup> It received still further confirmation from the animal experiments of Planer in 1860,<sup>40</sup> who found that the stomach absorbed oxygen and secreted carbon dioxide in the proportion of two parts of the latter to one of the former. Subsequently, however, the view that a direct secretion of CO<sub>2</sub> takes place was abandoned, and it was generally assumed that the oxygen and the nitrogen of the stomach gases come from the swallowed air, whereas the CO<sub>2</sub> arises from the blood by simple diffusion. In 1892 Schierbeck<sup>45</sup> made an important series of experiments, using the method described at the beginning of this section. This author found that CO<sub>2</sub> is always present in the stomach and that its tension varies directly with the stage of digestion. Beginning with 30 to 40 mm. in the fasting animal the CO<sub>2</sub> tension rises to 130 or 140 mm. at the height of gastric activity. Schierbeck therefore rejects the view that the CO<sub>2</sub> results from diffusion (for its tension in the cavity of the stomach is far higher than it is in the gastric vessels\*) and concludes that the gas is an expression of the metabolic activity of the gastric mucosa. In other words, he has furnished a strong experimental basis for the old theory of alimentary respiration.

These studies have been extended by Giglio,<sup>18</sup> who found that the production of CO<sub>2</sub> is considerably influenced by the kind of food ingested, the carbohydrates causing the greatest production of the gas, the fats the least. In normal dogs he could not confirm the classic 1 to 2 ratio of Planer, but found values ranging from 1 to 1.30 to 1 to 0.67 according to the diets used.

From the work quoted it cannot longer be doubted that some of the gas (CO<sub>2</sub>) normally present in the stomach arises from the gastric mucosa itself. What evidence is there that this gas may at times be produced in such amounts as to cause gross pathological accumulations? Bardet<sup>2</sup> has studied 2 cases of occasional flatulence. He recovered 20 to 50 liters of gas in one hour, and this gas contained on an average: CO<sub>2</sub>, 80 per cent.; O, 7 per cent.; N, 13 per cent. Woodyatt and Graham<sup>53</sup> found in a case of acute gastric dilatation: CO<sub>2</sub>, 24 per cent.; O, 4 per cent.; N, 72 per cent. Experimentally Schierbeck<sup>46</sup> showed that the low CO<sub>2</sub> tension of a fasting animal could be increased by injections of pilocarpin and that the high tension of a fed animal could be depressed by injections of nicotine. A high CO<sub>2</sub> tension persisted unchanged after vagus section. Unfor-

\* The average CO<sub>2</sub> tension of arterial blood is 35 mm. Hg. (Howell<sup>54</sup>).

tunately, further direct experiments on the nervous control of gas production are wanting.\* The entire question must really be studied much further before we can speak with real confidence of these abnormal gas productions.

### III. THE ENTRY OF AIR INTO THE STOMACH; AIR-SWALLOWING.

If any sufficiently large group of individuals be examined it will be found that perhaps a majority will recall that they belch after eating.† A smaller number will be able to belch on request. A very few may be able to swallow air when asked to do so. In addition a certain proportion will be found to be unconscious belchers and air-swallowers, whereas a final group will be quite unable to belch or to swallow air even after making every effort to acquire the practice. It is important for the student of the physiology of air-swallowing to bear these facts in mind, for we are about to enter a field in which there is every gradation between the distinctly conscious or volitional on the one hand and the subconscious, automatic or reflex on the other. It is not without reason that the French have described aerophagia as an unconscious voluntary act. This apparent paradox is essentially true, for in the first place no act of air-swallowing can be initiated without the participation of striped or voluntary muscle groups on the one hand, whereas it can be checked or prevented by the influence of the will on the other; and in the second place the process may be repeated so often that it becomes a habit and thus passes into the realm of the subconscious, where it is no longer recognized as a distinct procedure by the subject.

\* In this connection it may be of some interest to recall the following observation. As is well known, certain fishes are supplied with air bladders (originally derived from the alimentary canal), and in some of these, highly vascular bodies known as red glands or gas glands, are present. These bodies serve to regulate the interchange of gases in the bladder, and this rudimentary or secondary respiration has often been pointed to as being analogous to the alimentary respiration of the higher vertebrates which we have been studying. A very elaborate study of the function of the air bladder was undertaken by the French zoölogist Moreau.<sup>28</sup> This worker made the interesting discovery that section of the sympathetic nerve to the swim bladder causes an increased production of oxygen, whereas section of the vagus does not affect the oxygen content.

† Among the Orientals, belching in public is not considered out of place, as with us. Thus Morange writes:<sup>29</sup> "Un de nos amis, officier d'infanterie coloniale, ayant pris part à la récente campagne de Chine, nous décrivait comme suit le cérémonial de la fin d'un diner chez un riche mandarin: après le défilé d'une trentaine de plats et l'absorption du riz traditionnel, l'amphytryon se lève et s'excuse auprès de ses invités de les avoir si pitoyablement traités, redoutant que leur faim ne soit pas complètement assouvie. Ceux-ci protestent alors avec véhémence, vantant la délicatesse, la variété des plats servis; puis, appuyant les mains sur le ventre, ils s'approchent de leur hôte et lui lancent en plein visage plusieurs rots bien sonores, témoignant ainsi que leur estomac est bien garni." The following quaint passage from a letter by Flaubert is also *à propos*: "Quelques fois nous nous arrêtons pour déjeuner dans un restaurant turc; là on déchire la viande avec ses mains, on recueille la sauce avec son plain, on boit de l'eau dans des jattes, la vermine court sur la muraille, et toute l'assistance rote qui mieux mieux, c'est charmant." (Quoted by Aubert<sup>27</sup>.)

Air may enter the stomach in one of two ways: It may either be carried down with fluids or solids in ordinary swallowing or it may be "gulped" down alone.

**THE SWALLOWING OF AIR WITH FOOD.** This method of air entry into the stomach occurs to a greater or a less degree in every individual. It is nearly always subconscious. In order to understand the mechanism of this process it is necessary to review critically and in some detail our knowledge of deglutition in general.

*The Mechanism of Deglutition.* Magendie<sup>113 114</sup> made the first classic studies on the subject and came to the conclusion that a bolus is propelled by peristalsis through three successive portions of the tract, viz., the mouth, the pharynx and the esophagus. Between the years 1880 and 1883 the Berlin physiologists, Kronecker, Falk and Meltzer, carried out a series of brilliant investigations which have served as the basis for our modern knowledge of the subject. Kronecker and Falk<sup>109</sup> found that at the moment of swallowing a pressure of 20 cm. of water is developed in the buccopharynx and that it is propagated onto the esophagus, but is absent in the stomach. Furthermore, by means of balloons in the pharynx and esophagus, connected with a recording drum, Kronecker and Meltzer showed that fluids were projected down almost instantaneously.<sup>110 112</sup> They then presented a theory of deglutition essentially as follows: The swallowing act is initiated by a contraction of the mylohyoids, which develop enough pressure to "squirt" the bolus down the entire esophagus without the aid of peristalsis. After the passage of the fluid the esophagus begins to contract until, at about six seconds, the "wave" reaches the cardia. This contraction serves simply as a reserve means of clearing the esophagus of the last remnants of the original bolus. Further graphic studies were contributed by Schreiber,<sup>126 127 128</sup> who showed that before the esophagus opens to admit the bolus a considerable negative pressure is developed. Instead of reaching the cardia in one-tenth second, as Kronecker and Meltzer supposed, it takes almost two seconds for this period of the act, a figure more nearly in accord with roentgen-ray observations. This first stage of swallowing was studied in greater detail by Kindermann (with Zwaardemaker) (1903),<sup>106</sup> who proposed to divide the entire act of deglutition into two main periods, a buccopharyngeal and an esophageal. The buccopharyngeal period is further subdivided into three phases (*Einstellungsphase*, *Austrreibungsphase* and *Regressivphase*) according to the role played by the floor of the mouth, the soft palate, the hyoid bone, the larynx, and the epi- and mesopharynx.

The next important physiological observations were contributed by clinicians. The surgeon, v. Mikulicz,<sup>129</sup> became attracted to the subject through his interest in esophagoscopy. He showed that the esophagus is open and air-containing from the level of

the larynx to the cardia, and that the pressure within the lumen is normally from  $-0.5$  to  $-3$  cm. of water (Schlippe, working independently, gives practically the same figures).<sup>125</sup> Fluids may pass through the cardia into the stomach without the aid of any factor other than gravity alone. In a very thorough study, based on anatomical, pathological and clinical grounds, the laryngologist Killian showed (1908)<sup>105</sup> that the top of the esophagus was closed off from the hypopharynx not only by the dead weight of the opposed larynx but by a very real, tonically contracted sphincteric musculature. To this he gave the name "mouth of the esophagus," and found that it relaxed, by an inhibitory reflex, only on swallowing, retching and vomiting.

The first roentgen-ray observations were made in 1898 by Cannon and Moser,<sup>98</sup> who showed that fluids were projected rapidly (squirted), whereas solids and semisolids were propelled more gradually by peristalsis. These studies were followed by those of Eykman (1903),<sup>99</sup> who directed his attention entirely to the buccopharyngeal period of deglutition. Further roentgen-ray observations have been reported by Hertz (1907),<sup>102</sup> Schieier (1911),<sup>124</sup> Schreiber (1911),<sup>127</sup> Kraus (1912),<sup>107</sup> Held and Gross (1906)<sup>101</sup> and Hirsch (1916).<sup>104</sup> The work of Kraus is particularly important. This observer found, by means of roentgen cinematography, what had indeed been described earlier by Hertz, namely, that the esophageal period is really of more importance than earlier writers had assumed. Instead of the bolus being squirted through the cardia with the initial buccopharyngeal thrust, it passes but slowly into the stomach under the pressure of the esophageal "peristole," and is followed invariably by a bubble of air. It is only by means of a nice interplay of cardiac relaxation and esophageal peristalsis that the bolus is finally delivered into the stomach.

Reviewing the above descriptions of the act of deglutition in the light of his own fluoroscopic observations the writer has come to agree thoroughly with Kraus in his statement that too little importance is generally attached to the phenomena associated with the cardia. This is undoubtedly due to the difficulty encountered in studying this region before the application of the roentgen rays to clinical physiology. It would seem perhaps more in harmony with the latest studies to speak of the swallowing act as composed of three, rather than two, chief periods, viz., a buccopharyngeal period, an esophageal period and a cardiac or cardio-gastric period. This would bring into greater prominence such important work as that of Müller and Saxl (1908),<sup>121</sup> who suggested that both the rearrangement of the individual muscle fibers and the relaxation of their tone is due to a reflex from swallowing; as well as that of Cannon and Lieb (1911)<sup>97</sup> who studied this phenomenon experimentally in man and animals, and gave it the happy designation of "the receptive relaxation of the stomach." In other



words, the act of deglutition is consummated, not with the arrival of the bolus in the esophagus or at the cardia, but with its penetration into the stomach; and the preparation of the latter organ is just as much a part of the process as are any of the phenomena heretofore considered. In fact, we are dealing with an orderly progression of pressures and inhibitions which may be presented, so far as they are known, schematically, as follows:

- A. Pressures: 1. Initial buccopharyngeal thrust (Meltzer and collaborators).
- 2. Esophageal peristalsis (Magendie, etc.).
- B. Inhibitions: 1. Inhibition of esophagus mouth (Killian).
- 2. Relaxation of esophagus (Schreiber).
- 3. Inhibition of cardia (Meltzer).
- 4. Receptive relaxation of stomach (Cannon).

From this new view-point, then, the known facts of deglutition may be summarized as follows:

**Buccopharyngeal Period:** The mouth is closed off anteriorly by the rise of the base of the tongue, the nasopharynx by the rise of the soft palate. The larynx advances and is sealed by the epiglottis and the back of the tongue. The bolus is thrust down by the contraction of the mylohyoids chiefly. This period is completed with the return of the larynx to its original position and is over in less than a second (seven-tenths to one second—Kraus).

**Esophageal Period:** This period begins almost immediately with the discharge of the deglutition reflex by a relaxation of the entire esophagus. At two-tenths second (Schreiber) the esophagus mouth opens just long enough to receive the bolus. After the entry of the latter, peristalsis begins at the closed esophagus mouth and forces down the bolus with its accompanying air bubble. This period ends with the arrival of the wave at the cardia and lasts six to seven seconds in all.

**Cardiogastric Period:** This period also begins with the discharge of the deglutition reflex, by an inhibition in the tone of the cardia (Kronecker and Meltzer) and a relaxation of the stomach. According to Cannon the lowest point of intragastric pressure is reached at approximately the time when a bolus is delivered into the stomach by the esophagus. After the relaxation, which requires about ten seconds for its full development, there is a rapid recovery of the former tonicity.

It is thus seen that the successive periods overlap, in this way providing for a practically continuous passage of the bolus. The only delay is at the cardia, where the relaxation is never complete enough, normally, for a discharge of the bolus, *en masse*, into the stomach.

**Swallowing Sounds.** On auscultating an empty stomach in the epigastric region during a single swallow of fluid a very characteristic

sound is heard six to seven seconds after deglutition. This phenomenon was carefully studied by Meltzer\* (1883),<sup>116</sup> and was called by him "*Durchpressgeräusch*." It has become known in the literature also as the "second swallowing sound." Meltzer found that the interval elapsing before the sound was heard corresponded to the time necessary for the wave of esophageal peristalsis to reach the cardia, and he therefore formulated his theory that the bolus, after being shot rapidly through the esophagus, was held up until the succeeding wave of peristalsis forced it into the stomach. If the cardia was relaxed—as was found to be the case in a small minority of individuals—the food went through at once, and a short "*Durchspritzgeräusch*" ("first swallowing sound") was heard correspondingly earlier. The same author also pointed out (1884)<sup>117</sup> that the sound was not heard over the filled portion of the stomach, and that as more food was ingested the murmur became fainter (higher pitched), and finally quite inaudible. Zenker (1884)<sup>130</sup> was the first to advance the theory that as each bolus reaches the cardia it separates into two parts, the fluid constituents going through first, the air following later with a murmur. As proof, he brought forth the fact that in an inverted subject the murmur is heard immediately after swallowing. In 1887 Quinke furnished still more elaborate experimental evidence<sup>123</sup> that the swallowing sound was due to the entrance of air into the stomach. Experimenting with narcotized dogs, he introduced a tube through the esophagus to a point somewhat above the cardia. This tube was attached to a burette in such a fashion that air or water could be introduced at will. It was found that if a normal-sized bolus of air or water was delivered into the esophagus by this means it was promptly propelled into the stomach by the so-called secondary peristalsis of Kronecker and Meltzer<sup>112</sup>—peristalsis not associated with a previous deglutition. When water alone was introduced no swallowing sound was observed; only when air had been previously admitted was the murmur audible. Quinke concluded that the character of the swallowing sound depended upon the amount and consistence of the bolus as well as upon the size and position of the air space in the stomach.

The first roentgen-ray studies of the swallowing sounds were made by Hertz (1907).<sup>102</sup> This author experimented on a group of healthy men and observed that certain changes in the character of the sounds were associated with changes in the position of the

\* The first author to mention this sound was Natanson (1864),<sup>122</sup> but his description was very incomplete. Hamburger made an elaborate study of the auscultatory phenomena of swallowing (1868),<sup>100</sup> but listened to the esophagus from behind and did not hear the sound. Allbutt follows Hamburger entirely (1875).<sup>95</sup> The only one who can claim priority to Meltzer was Zenker who described the murmur accurately in 1869.<sup>129</sup> His original paper appeared in a small psychiatric journal and did not receive general recognition.

body. Although he correctly observed that the second swallowing sound was heard just after the food had left the esophagus he failed to give any satisfactory explanation for the phenomenon. Kraus (1912)<sup>107</sup> was apparently the first roentgenologist to make the positive observation that the swallowing sounds are caused by the penetration of air into the stomach, but he has published no detailed account of the subject.

*Experimental.* In view of the above rather unsatisfactory state of the literature the writer undertook a study of the problem with the aid of the fluoroscope, hoping in this way to establish more precisely the relation between the swallowing sounds and the entry of air into the stomach. As subjects, ten healthy men were selected. These were examined fasting. At practically every session a complete standard opaque meal—100 gm. barium sulphate in two glasses (500 c.c.) of fermented milk—was given so that the conditions could be observed in each individual at every stage of gastric filling. Twenty-one observations were made in this series. The exact procedure was as follows: The subject was placed behind the screen and a preliminary fluoroscopy made in order to note the presence of a fasting *Magenblase* or other gas accumulation in the abdomen. The first glass was then given to the subject to hold in readiness, and he was told to make a single deglutition at the word "swallow" and to strike the operator at the exact time the order was carried out. It was found essential to adopt some such method of announcing the execution of each swallow (whether by command or involuntarily), as it would otherwise have been impossible for the observer to interpret correctly the phenomena occurring at the cardia. Finally, the stethoscope was adjusted in position, the rubber tubing being long enough to reach under the screen to the epigastric notch of the subject. The observations were made with the subject standing directly or obliquely in front of the tube\* or lying supine or obliquely above it. Holzkecht's first oblique position was the one adopted (right shoulder to tube posteriorly, left shoulder to screen anteriorly).

The chief findings may be presented as follows: in general, the bolus is found to reach the cardia in one or two seconds, depending presumably on the amount swallowed and the force employed in the effort. As a rule the food begins to penetrate the cardia in a thin stream without any appreciable delay whatever. In several instances the bolus was held up at the cardia either as a whole or after part had gone through. This was due to causes which cannot be gone into here. In every case examined a bubble of air was seen at the top of the food column (Fig. 1), and in many instances a distinct *niveau* (air above fluid) was in evidence. No peristaltic waves could be made out at any time, the barium column seeming

\* By means of the Coolidge tube (Scheidel-Western "Peerless" transformer); practically continuous observations lasting one-half hour or more, were possible.

simply to sink down into the stomach.\* In every case in which the second swallowing sound was heard it occurred immediately after

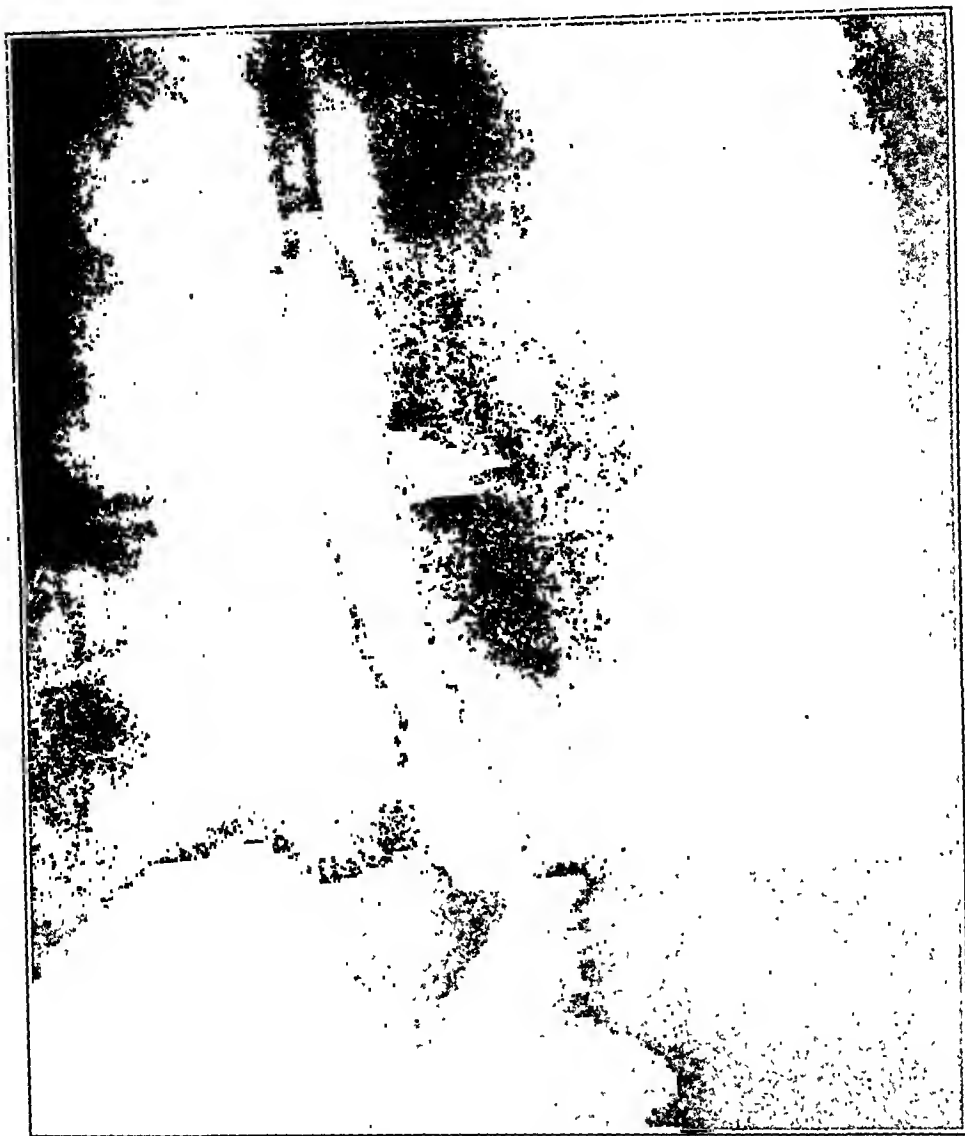


FIG. 1.†—Normal air-swallowing. First oblique position (Holzknecht). Exposure at two seconds after deglutition. Gas present in stomach from previous swallowing. Food column occupies more than half of thoracic esophagus. Narrow stream trickling through cardia. Air bubble above food (no *niveau*).

\* On the occasions when a delay occurred at the cardia, there often appeared a rather violent and repeated contraction of the lower part of the esophagus, whereby the *niveau* (when present) was obliterated, the food column narrowed, and the bolus itself propelled for a variable distance up the thoracic esophagus. In such cases, the second swallowing sound was delayed until the spasm was relaxed and the esophagus had expelled its food content. In the most marked instance recorded, the sound was not heard until more than sixty seconds after the original deglutition.

† In taking these plates a rather soft tube was used and exposures were made as short as possible to bring out detail in left diaphragm. The *Magenblase* was generally taken during expiration. Abdominal pressure was avoided so far as possible. The subject was of course always standing, distance of plate from anode being twenty-four inches.

the disappearance of the last portion of food through the cardia. It was, of course, impossible to recognize as such the passage of air into the stomach when this preceded, and in many cases even when this followed, the opaque shadow; but whenever a bubble of air was completely incorporated within the bolus the characteristic sound was heard as it passed the cardiac boundary. In the reclining

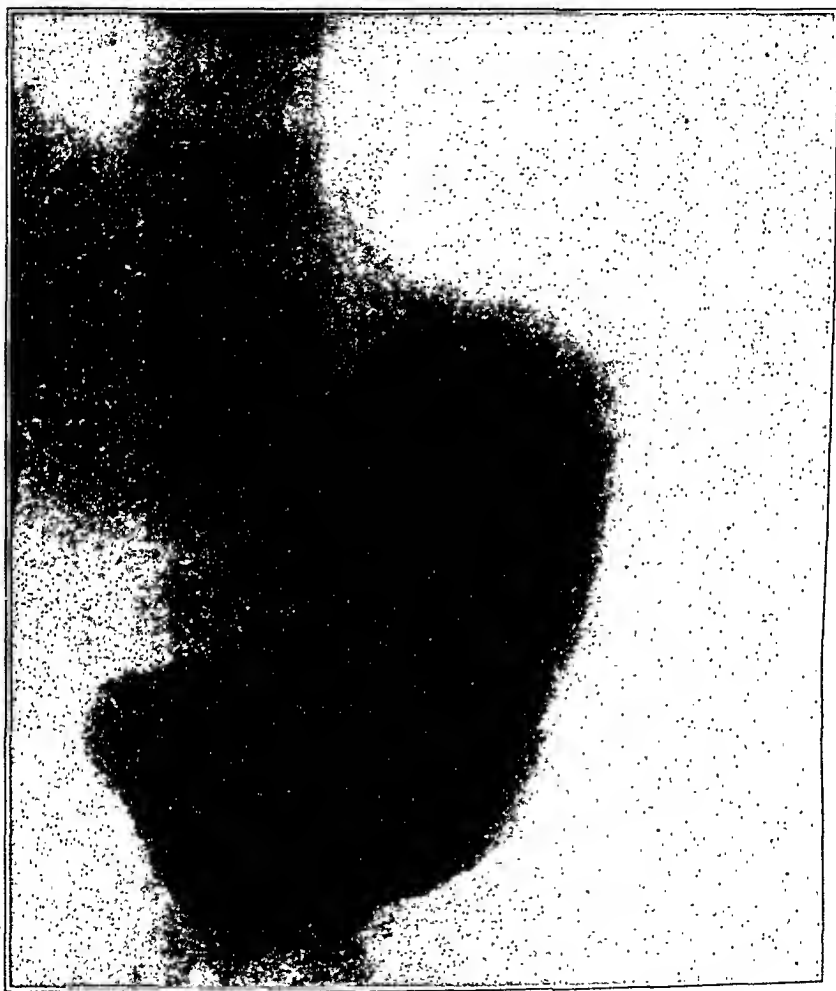


FIG. 2.—Normal *Magenblase* before belching. Same individual as Fig. 3.

position, as might be expected, the whole process of deglutition takes longer. The bolus reaches the cardia in from two to four seconds and does not leave the esophagus completely for eight to thirteen seconds. In this case, as a rule, more than one swallowing sound is heard. Very often a murmur occurs at the beginning of cardiac passage in three or four seconds. Next a succession of sounds may appear at intervals as air mixed with the food passes the cardia. Finally, with

the complete disappearance of the bolus, an entire series of squirts may be heard, at times interrupted by acts of inspiration.

It follows from the above observations that the production of swallowing sounds is due chiefly to two factors. The first is the presence of air in the bolus; the second is the force of gravity. In other words, the time of occurrence as well as the number of swallow-



FIG. 3—Same individual as Fig. 2, after belching. Note: changed position of diaphragm, small amount of residual air in stomach; change in shape of food column (narrower and longer), and small bubble of air at top of duodenal cap.

ing sounds depends entirely upon the position and distribution of the air contained in the bolus. A third factor plays a role of almost equal importance. If the cardia is open when the food arrives it is possible for (some of) the air to precede the bolus, and we then have the first swallowing sound just as Meltzer described it. If the cardia is relatively contracted, as is more often the case, there is time, in

the erect posture, for all the air to rise to the top of the fluid, and then only one—the second—swallowing sound is heard.

Let us now direct our attention to the gastric side of the picture. In the fasting condition, as a rule, no distinct *Magenblase* is dis-



FIG. 4.—Stomach of air-swallower filled with standard barium meal. Note amount of air swallowed with food.

cernible. Only an indefinite light area can be made out in the region of the fornix. With the very first swallow, however, a clearly defined bubble of air appears in the stomach. This, with the opaque food below it, gives the typical roentgen appearance of initial gastric

filling, viz., a light semicircle capping a dark inverted triangle. With each successive swallow the *Magenblase* increases in dimensions. Here an important distinction must be noted. In the hypersthenic or stout members of the group examined, with their high-placed, oblique stomachs, the *Magenblase* became flatter and flatter until it appeared above the horizontal food level as a broad but very shallow segment of a very narrow oval. In these cases the swallowing sound,

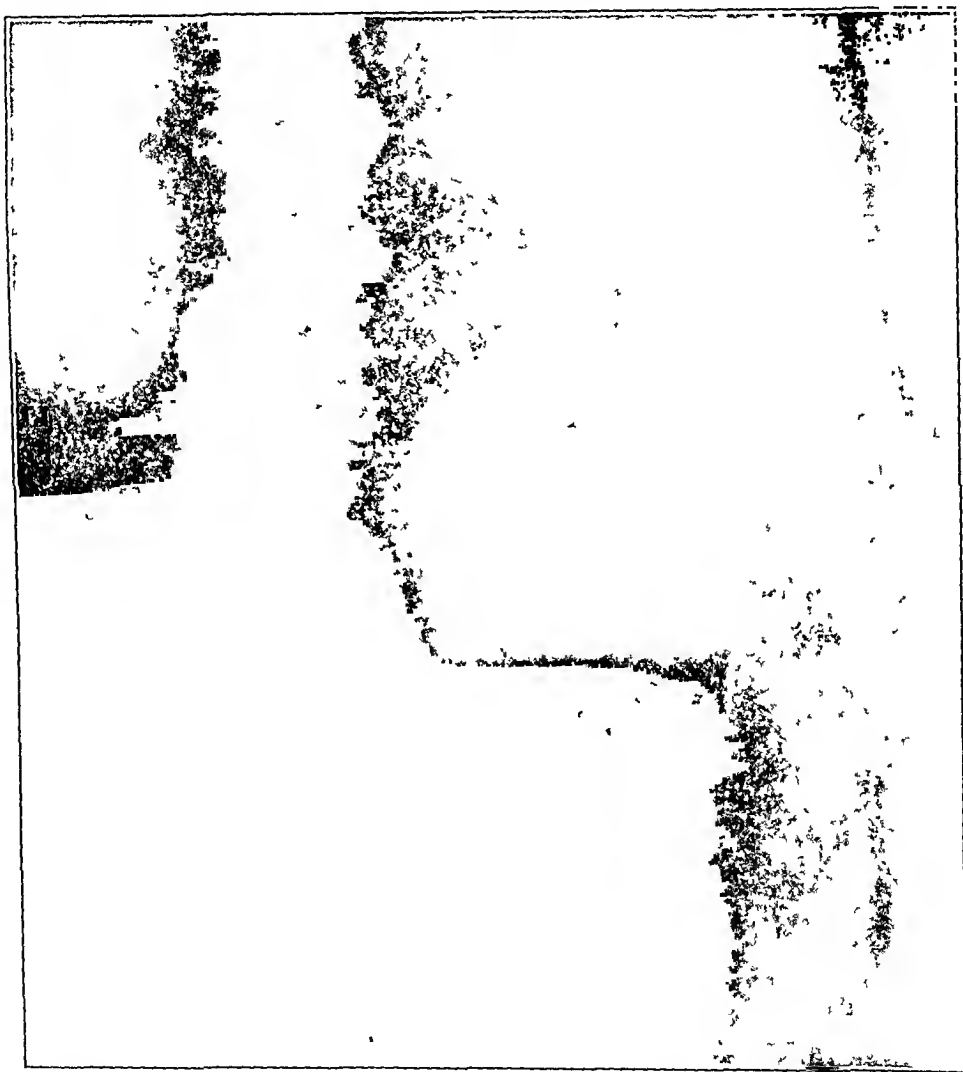


FIG. 5.—Same individual as Fig 4 (air-swallower). Standard barium meal with six additional deglutitions of air. Note thinning and elevation of left diaphragm.

never very loud, became rapidly higher pitched and fainter, until by the time the first glass was consumed (250 c.c.) the murmur was generally inaudible. As soon as belching occurred, which was usually early, the swallowing sound was restored. On the other hand, in the slim, relatively asthenic individuals, with long, narrow, ptotic stomachs, the *Magenblase* reached a larger size, retaining its rounded form, or becoming actually pyramidal, with the apex downward.



The swallowing sound was loud and persisted practically unchanged throughout the entire filling.

So far we have considered what takes place with single swallows of fluid.\* When repeated deglutitions are made, as in ordinary



FIG. 6.—“Gas splint.” No swallowing sounds. Note accumulation of gas in distal colon compressing stomach. Patient with constipation.

swallowing, relatively less air is admitted into the stomach. The actual amount of gas ingested seems, again, to depend upon the behavior of the cardia. If the latter is relatively patent, a clear space

\* It may be of interest to mention that Duroziez<sup>23</sup> used this method—“faire boire le malade a petits coups”—in order to create a zone of resonance against which the lower border of the heart could be percussed out.

(air) can generally be made out between two successive food masses. In this case a swallowing sound is heard after each deglutition. If, as is more commonly the case, the cardiac relaxation is less complete, the food column is added to by each successive swallow until the esophagus is filled almost to its mouth. In this case a relatively small amount of air is admitted, and but a single swallowing sound is heard when all the food has entered the stomach.

One further observation is of importance. If there is a large accumulation of gas in the distal (*i. e.*, terminal part of transverse splenic and descending) colon (Fig. 7) no swallowing sound is heard, at least until after a considerable amount of food is ingested. This finding was particularly marked in patients with constipation and intestinal flatulence. The most reasonable explanation of this phenomenon is that such gas accumulations pad or splint the stomach in such a way as to prevent that degree of vibration necessary for the production of a murmur. That the audibility of the swallowing sounds depends to a definite extent on the tonus of the gastric musculature is borne out not only by the previously described difference between the hypertonic and the subtonic cases, but by the additional fact that in the reclining posture (in which the gastric wall tension is presumably lessened) the most hypertonic cases will present loud and reverberating swallowing sounds.

THE SWALLOWING OF AIR ALONE; "AIR-GULPING." Several observers have described their personal experiences with air-swallowing. Magendie<sup>76</sup> learned the practice himself and taught it to twenty of his students. Weissgerber<sup>94</sup> was the first to publish a detailed account of the mechanism he followed.

*The Mechanism of "Air-gulping."* The writer taught himself to swallow air by following Weissgerber's directions. In performing an ordinary esophageal eructation—that type of eructation subject entirely to voluntary control—two distinct steps are involved. In the first of these the air normally present in the pharynx is forced for a varying distance into the esophagus. In the second step—which follows immediately after the first—the air is rejected by increasing the intrathoracic and intraesophageal pressure as the result of an act of forced expiration with closed glottis. Both these phenomena are associated externally with a rise and fall of the larynx, a movement which is more rapid and more marked in the first instance, slower and less evident in the second. Two sounds also accompany the act. In the first step, the mouth being closed, the sound is muffled; in the second step, the mouth being generally open and the soft palate vibrating, the sound is correspondingly louder. It is not difficult to learn to dissociate these two phenomena, and ultimately, by suppressing the second, to prevent the escape of air from the esophagus. If now, after executing the first movement, an ordinary "empty" swallow be taken, the air previously forced into the esophagus will be propelled by means of peristalsis

into the stomach. That this is actually the case is shown by the following experiences:

1. Immediately after the swallow a sense of constriction (the degree depending upon the size of the air bolus) was noted in the upper chest, and felt to travel slowly down toward the epigastrium. The feeling is similar to that accompanying the ingestion of too large a piece of food. That the sensation in the latter instance is due to accompanying peristalsis was shown by Hertz<sup>103</sup> in the course of his experiments on sensations in the esophagus.

2. If the epigastrium was auscultated during this experiment a loud murmur was heard two to four seconds after the deglutition. With the appearance of the sound a sense of relief from constriction was experienced.

3. The procedure was repeated, under simultaneous fluoroscopic and auscultatory observation, by one of the subjects of experiment. Coincident with the occurrence of the swallowing sound a large bubble of air was seen to enter the stomach.

4. After repeated deglutitions in the manner described a moderate sensation of distention was experienced. This sensation was relieved after a spontaneous, gastric eructation.

5. Several deglutitions were performed with the mouth and throat full of tobacco smoke. The smoke was not inhaled into the lungs. After an interval, sometimes as long as several minutes, smoke was belched out of the stomach.

It is not absolutely necessary, however, to execute an accessory swallowing movement in order to bring air into the stomach. If the first stage only of an esophageal eructation be executed the air introduced into the top of the esophagus will be propelled downward by the secondary peristalsis so thoroughly investigated by Meltzer,<sup>112 119</sup> Cannon,<sup>16</sup> Quincke<sup>123</sup> and others. Furthermore, if sufficient force be used, and *especially if the cardia be relaxed at the time*, the air may be squirted into the stomach directly, without the intervention of peristalsis, as was originally suggested for the ease of fluids, by Kronecker and Meltzer. That this is more than a mere possibility seems evident from the observations made on two of the subjects of experiment, both adepts at air-swallowing. Under simultaneous fluoroscopy and auscultation the air was both seen and heard to enter the stomach within two seconds after the beginning of the act. Moreover, there was no sense of peristalsis experienced by the subjects under these conditions. Indeed, it is by no means unlikely that many of the air-swallowers and belchers met with clinically are cases of (perhaps voluntary) relaxation of the cardia.

In order to describe this mechanism of air entry into the stomach, and to distinguish it from the swallowing of air with food, the term "air-gulping" seems preferable to any other. As already suggested this is, in the writer's opinion, the ordinary maneuver practised by air-swallowers, whether their digestions be healthy or disordered.

However, there has been a tendency among certain writers (Quincke (1889),<sup>86</sup> Pitres (1895),<sup>85</sup> Linossier (1901),<sup>73</sup> Soupault (1906),<sup>90</sup> Cade (1910)<sup>61</sup>) to regard as essential certain respiratory phenomena said to accompany the act of air deglutition. Indeed, the term "air inspiration" has achieved a certain popularity, and graphic studies have been undertaken (Chatin and Tremblay, quoted by Cade<sup>61</sup>) to show the part played by the diaphragm and other muscles of respiration during the process. A description of the act of aerophagia, according to this teaching, is as follows: The subject closes his mouth, lowers his chin and executes a movement of deglutition. This is accompanied or preceded by an inspiratory effort with closed glottis. In this manner the thorax is dilated, an increased negative pressure occurs in the esophagus and the intra-esophageal penetration of a bolus of air is facilitated.

Although the writer has obtained no evidence which would justify him in denying categorically the possibility (at least in certain cases) of "air inspiration," it should be mentioned that in the course of his fluoroscopic observations it was definitely noted that air could be swallowed with the diaphragm in deep expiration just as well as in deep inspiration. Furthermore, it seems quite certain that a simple deglutition ("empty swallow"), unassociated with an actual gulping of air, does not introduce any appreciable amount of gas into the stomach no matter what the intrathoracic pressure relations may be. Now, as it is absolutely essential for the esophagus mouth to be relaxed before anything can pass into the gullet (Killian), some reflex mechanism other than swallowing (which does not introduce air) must be invoked for this purpose. Thus, to be sure, it is conceivable that an inhibition with gaping of the esophagus, such as Killian has observed in gagging or retching, may take place. So far, however, no work has been done with this possibility in mind, and it seems therefore best to regard the case for "air inspiration" as not yet proved.

*Experimental.* Two of the ten subjects examined were skilful air-swallowers. It was found that but five or six gulps were sufficient to distend the fornix and tubus of the empty stomach, and in some cases, though much less fully, the pyloric vestibule as well. The left diaphragm was raised considerably to a point about 2 or 3 cm. above the level of the right. The gulping of air into the filled stomach not only raised the diaphragm but caused a depression of the food level as well, with an associated broadening of the stomach through the tubus (Fig. 5).

In some cases, as already mentioned, air would penetrate the stomach practically at once after the gulp. Here a wide relaxation of the cardia was assumed. Where the passage took longer the aid of peristalsis was invoked. It was found that although the peristalsis was associated with a sense of constriction in the standing posture this sensation was absent reclining, even when the air did not

enter the stomach for as long as three seconds. In general, also, it was much easier to swallow air in the recumbent than in the standing position.

#### IV. THE FATE OF AIR IN THE STOMACH.

**BELCHING.** The greater part of the air introduced into the stomach escapes through the esophagus by eructation. This act has been shown by v. Mikulicz<sup>120</sup> and others to be a true reflex, and necessitates an inhibition of the normal tonic contraction of the cardia.\* The factors bringing about this inhibition are many and interesting, and have been the subject of much investigation.

*Intragastric Pressure.* Kelling<sup>69</sup> has found that belching occurs whenever intragastric tension reaches 25 cm. of water. Under ordinary conditions of swallowing the receptive relaxation of the stomach (Cannon) provides for a *fall* in intragastric pressure. What then are the factors which may occasion such a rise as that found by Kelling? In the first place it is generally agreed that the pressure within the stomach increases as digestion progresses (Dobrovici),<sup>62</sup> and it is quite possible that during the contractions associated with active peristalsis some gas may be forced through the cardia. Furthermore, it should be borne in mind that a bolus of air differs from a solid or fluid bolus in that it increases in size after its introduction into the stomach owing to the difference in temperature between the atmosphere and the interior of the body. A simple calculation shows that whereas outside air swallowed in summer (80° F.) would increase by 4 per cent. of its volume, the same amount of air swallowed in winter (40° F.) would increase by 12 per cent. of its volume.

*Gastric Hyperesthesia.* It has already been suggested that in individuals with hypertonic stomachs, belching of air swallowed with food occurs earlier than in those with more lax gastric musculature. This is the general rule, and is the common experience in examining patients by means of the fluoroscope. That the question is not entirely one of gastric tonus, however, was suggested by the reactions of the two air-swallowers in the series examined by the writer. Both of these individuals were of the slim build, with long stomachs reaching below the level of the iliac crests. Whereas one of the subjects could store relatively large quantities of air in his stomach with little distress and for long periods, the other, who incidentally presented the greater ptosis, was so inconvenienced by the presence of air in his stomach that he was forced to belch after every five or six deglutitions. We may speak of this individual as being hypersensitive to gas. In the experimental

\* It is extremely likely that there is an inhibition of the esophagus mouth as well. Killian,<sup>105</sup> who has observed this to occur in vomiting, mentions nothing of the behavior of this sphincter during eructation.

study undertaken by Dobroviei, it was found that in a series of 18 air-swallowers the greater number (13) showed this peculiar hyperesthesia of the stomach to distention, whereas the other 5 could stand an intragastric pressure of 20 to 25 cm. without much discomfort.

*Posture.* Belching is aided by the erect posture or by lying on the left side. The act is difficult or impossible in the right lateral, the prone, the supine or the inverted postures.

*Acidity.* Cannon described the acid closure of the cardia.<sup>96</sup> At the beginning of digestion this sphincter showed frequent relaxation with regurgitation of stomach contents. As the acidity rose, these regurgitations ceased. These findings in animals were confirmed by the following personal experience. Some air was swallowed and then about 15 c.c. of  $\frac{N}{10}$  HCl was ingested. The usual eructation did not take place: the gas had been effectually sealed in the stomach. However, soon after a corresponding amount of alkali (NaOH) was taken the air began to make its way out through the esophagus.

*Peripheral Reflexes.* It is an old clinical observation that the stimulation of certain distant parts of the body, particularly in "neurotic" individuals, may provoke eructations. Thus, Frank (1842)<sup>66</sup> reports this effect from the pressure of the forearm in an old man, from feeling the pulse in a woman, from the movements of the waltz in a young girl. Mathieu and Follet,<sup>77</sup> Bouveret,<sup>59</sup> Leven,<sup>71</sup> Soupault<sup>90</sup> have reported similar observations. In addition to seeing such an instance of "eructogenic zone" at the epigastrium the writer had the opportunity of observing a very interesting phenomenon in a woman with a sinus leading to the liver. When barium paste was injected beyond a certain amount the patient was seized with a desire to eructate. We have here a rather striking analogy to the clinical association of belching with affections of the biliary passages.

*Belching and Aerophagia.* As already indicated, esophageal differs from gastric belching in that the former is voluntary, whereas the latter is not. The esophageal belch is further to be distinguished from the other by the characteristic that it is a double phenomenon in which the gulping down of air precedes its expulsion from the gullet. Individuals subject to flatulence have used this voluntary esophageal belching as a means of provoking spontaneous gastric eructations. By what mechanism is this accomplished? To be sure, it is conceivable that the expulsive effort (constituting the second step of the artificial eructation) may be performed just at the moment when the cardia is relaxed by the gulp, in which case the gastric gases should be expelled summarily. As will be shown presently it takes but a very few eructations to evacuate even large gas accumulations. That this does not take place in the case under discussion is strongly suggested by the fact that these

efforts are repeated again and again by the patient. What is indeed much more likely is that the second step of the eructation not only fails to remove all the air from the esophagus, but that the residue is really carried into the stomach. Mathieu,<sup>78</sup> who auscultated these cases, actually heard the gurgle accompanying the passage of air through the cardia, a finding which the writer has confirmed on more than one occasion. In this way the patient (unintentionally, of course) introduces additional air with each successive "eructation," until the intragastric tension becomes so great that spontaneous gastric belching occurs and brings relief. It is for this reason that all persistent belchers should be regarded clinically as air-swallowers.

*Inhibition.* In the course of our experiments it was found that one of the subjects could inhibit an impending spontaneous eructation by swallowing more air or by executing a simple deglutition. In this case it may be assumed that the intragastric tension was depressed as described by Cannon. That the discharge of the deglutition reflex is associated with a general inhibitory effect was one of the earliest observations published by Meltzer.<sup>111 115</sup>

*Experimental.* The two air-swallowers were fluoroscoped while trying to assist or provoke gastric eructations. The diaphragm was depressed to the limit, the abdominal wall was pulled in, and the intra-abdominal pressure was further increased by flexing the thighs on the abdomen and bending the trunk forward. When these manipulations were successful the middle field (space between the heart and the spine in the oblique position) would light up brightly, indicating the passage of a large amount of air up the esophagus. At the same time the characteristic sound would be heard and the *Magenblase* would practically disappear, the food level rising, and the left diaphragm descending, to its normal position. As a result of these changes the entire stomach becomes shorter and narrower than before, whereas the food column itself becomes correspondingly longer. Even the largest gas accumulation is almost entirely evacuated after five or six belches, while the ordinary *Magenblase* noted after the ingestion of a standard opaque meal is generally brought up in a single eructation (Figs. 2, 3 and 4).

*PASSAGE INTO THE INTESTINE.* When air is swallowed with food in the erect position there is very little opportunity for the former to go through the pylorus. As already mentioned, by far the greater part is belched up long before the rest of the stomach contents are evacuated. In the reclining position the entrance to the pylorus seems more accessible.

On the other hand, if air is swallowed on an empty stomach, the gas may make its escape through both outlets. The following fluoroscopic observations were made on one of the air-swallowers. Six gulps of air were taken on an empty stomach within a period

of thirteen minutes. One-half minute after the last deglutition a loud gurgle was heard over the pylorus (Meltzer's *Pylorusgeräusch*).<sup>117</sup> This was associated with some relief in the sensation of distention and with the appearance of light areas below and to the left of the stomach (gas in the small intestine). Following this a few eructations and a greater number of pyloric passages were recorded. The latter were aided by deep inspirations or by bending forward. Certain loud gurgles, which were unaccompanied by a change in the sense of gastric tension, were ascribed to small intestinal peristalsis. The stomach was practically empty in forty-five minutes.

**ABSORPTION BY THE MUCOSA.** That oxygen is readily absorbed by the gastric mucosa is an old observation (see work of Planer and Giglio mentioned above). Recent studies have shown that the rate of this absorption is approximately 12 c.c. per minute (Yllpö).<sup>54</sup> It is therefore probable that whatever gas is passed into the small intestine at the end of an ordinary period of digestion consists chiefly of nitrogen with some CO<sub>2</sub> from the stomach. In the fasting stomach, however, whole air may pass through the pylorus. Yllpö reports that he experienced considerable flatulence two to four hours after the ingestion of air under these conditions, whereas the taking of large amounts of CO<sub>2</sub> and of O was not followed by this sensation. The difference, of course, is due to the unabsorbed nitrogen present in the first instance.

## V. SUMMARY.

1. In general, gaseous accumulations in the upper digestive tract have atmospheric air as their basis.

2. This air is introduced by ordinary swallowing or by an adaptation of the swallowing mechanism known as gulping.

3. The differences between the swallowing of air and that of food depend to a large extent on the influence of gravity. As a result the swallowing mechanism shows certain peculiarities which are described in this paper.

4. By means of fluoroscopic observations it can be demonstrated that the so-called swallowing sounds are produced by the entry of air into the stomach.

5. A close study of the mechanism of deglutition based upon a review of the literature and on original roentgen-ray observations shows the advantage of describing the complete act of swallowing as consisting of three instead of the classic two periods. These three periods are the buccopharyngeal, the esophageal and the cardiogastric.



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## VITAL STAINS AND THE CENTRAL NERVOUS SYSTEM.

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THE necessity for studies relative to the conveyance of substances to the central nervous system is indicated by the relative inadequacy of the treatment of quaternary syphilis by means of intravenous injections of arsenical preparations.

It has been assumed that substances introduced intravenously do not reach the cerebrospinal fluid or the brain. Failure to reach the cerebrospinal fluid has been accepted as the criterion of failure to reach the brain. This assumption has been reached through such investigations as have shown that arsenic, mercury and antimony do not pass the choroid plexus into the cerebrospinal fluid (Mott). Agglutinins of typhoid fever, bacterial toxins and hemolytic amboceptors do not enter the fluid. The explanation for this phenomenon has been sought for in many directions. *Intra vitam* staining of the central nervous system has been one of the principal method of research.

Trypan blue, a benzidine dye, was selected for experimental purposes because of the similarity of its physicochemical properties and its organotropic characteristics to salvarsan. Trypan blue when intravenously injected at first rapidly diffuses and gives an intense general stain to the tissue; finally, however, it is stored up in specific cells, the pyrrol cells.

Goldmann<sup>1</sup> has shown that after an intravenous injection of trypan-blue solution the brain and cerebrospinal fluid remains unstained. This observation has been confirmed by Frazier, Tilney, Woolsey, Hecht, Evans, one of us and others, and has been already remarked by Bouffard.

This singular action of the central nervous system has been explained in a number of ways.

Goldmann explained it on the basis of the filtering action of the choroid plexus. The fallacy of the conclusion is shown by the work of Bouffard, who found that following an intravenous injection of trypan blue when the brain remained unstained certain other tissues, as the ovaries and testes, likewise remained unstained. This has been confirmed by one of us (L. J. P.), by Evans, Schuleman and others. It has been found that the parenchyma of the testicle, the

<sup>1</sup> Arch. f. klin. Chir., 1913, ci, No. 3.

cortex of the suprarenal body, portions of the ovaries, the lungs and the brain remain unstained. Only certain cells, the pyrrhol cells, store up this stain, and other cells, as the epithelium of the convoluted tubules of the kidney, are free from stain, as are the blood cells.

It has been known from the work of Ehrlich, Heidenhain and Bethe, and lately has been shown by one of us (L. J. P.),<sup>2</sup> that certain other vital stains, as methylene blue and malachite green, enter into and may be demonstrated in the nervous tissue as well as in other organs following their intravenous administration. Some stains not necessarily of the composition of trypan blue, as fluorescein, cannot be demonstrated in the nervous tissue. Similar observations have been made by McIntosh and Fildes.

They found that with neutral red and alizarin blue the brain was stained, whereas the indigo carmine, light green, acid fuchsin, trypan red and blue and pyrrhol blue it was not. This difference in staining reaction of vital dyes could be due either to failure of the dye to reach certain tissues by reason of structural differences in the bloodvessels or, having reached these tissues, to a variation in the physicochemical reactions between the dye and the tissues.

Recently McIntosh and Fildes<sup>3</sup> argue that certain stains do not penetrate into the brain because the bloodvessels are impermeable to them. They state that the bloodvessels of the brain differ from those in other parts of the body in the possession of an extra-adventitial sheath. Among other conclusions they state that certain dyestuffs can pass directly from the blood to the brain substance without being found in the cerebrospinal fluid, and the inefficiency of certain dyestuffs in passing through the bloodvessels has nothing to do with their absence from the cerebrospinal fluid. They say that the chief factor which governs the passage of the dyes is their solubility reaction, which is not a general lipid solubility and corresponds to the solubility in chloroform and in water or perhaps to their partition coefficient in these liquids. MacCurdy<sup>4</sup> concluded that vital stains (trypan blue) must penetrate the vessel walls, albeit slowly.

Obviously, permeability of the bloodvessels determines only the capacity of a stain to come into contact with cells, and the degree of penetration into the cell is dependent upon other factors: (1) the permeability of the cell membrane; (2) the reaction of the cell contents to the stain as to solubility, partition coefficient, certain chemical relations of the fats and proteins within the cell and probably other factors.

If the absence of salvarsan from the central nervous system following an intravenous injection could be explained upon the same

<sup>2</sup> Proceedings of the Chicago Pathological Society, 1916.

<sup>3</sup> Brain, 1916, xxxix, 478.

<sup>4</sup> Psychiatric Bulletin, January, 1917, ii, No. 1.

basis as the absence of trypan blue under similar circumstances it must be due to a similar number of factors. McIntosh and Fildes<sup>6</sup> examined the brain of an infant dying after an intravenous salvarsan injection and found no arsenic present. Ullman, Morel and Mouriquad had similar experiences. They all concluded that salvarsan was not neurotropic, and Ehrlich accepted this opinion and concluded that salvarsan had no "Vorliebe" for the brain.

Having shaken 0.15 gm. of neosalvarsan with 100 gm. of minced brain, McIntosh and Fildes were unable to obtain that amount from a number of subsequent washings, and they concluded that their former opinion was wrong and that the brain fixed considerable neosalvarsan.

The fact that minced brain fixed a certain amount of neosalvarsan does not prove that living brain tissue would combine with it. In the latter case we are dealing not only with a mass of inert proteins, lipoids, salts, etc., but with living cells which, because of that very state, bind certain substances together, which in the combined state may refuse to take up matter for which they may have an affinity separately. A number of other factors must also be considered.

There are certain characteristics of vital stains in general and certain laws governing their action which, when reviewed, offer considerable assistance in the explanation of the absence of vital staining of the central nervous tissue with certain dyes.

Overton<sup>6</sup> in a study of vital stains found that stains possessing this property, as neutral red, methylene blue, thionin, etc., in contrast to the sulphonic acid dyes, as water-soluble indulin, nigrosin, anilin blue, etc., were soluble in oils, fats and fatty acids and readily soluble in lipoids, as lecithin, cholesterin, protagon and cerebrin. Furthermore, crumbs of these substances absorbed these vital stains from dilute solutions. He therefore concluded that the cell wall, probably consisting chiefly of lipoids, prevented the penetration of such substances as were insoluble in these lipoids.

Evans and Schuleman<sup>7</sup> point out the fact that although vital stains, the benzidine dyes are insoluble in fats or lipoids, and that the majority of the cells of the body are not surrounded by fat. They state that the diffusion power of a stain affects it merely by enabling the dye molecules to present themselves to the class of cells which will receive them. Having arrived at the cell the benzidine dye by no means diffuses into it, as is the case with various basic dyes (neutral red, methylene blue, etc.). The benzidine dyes filter in more slowly and never encounter physical conditions which favor their rapid spread.

Kite<sup>8</sup> holds that Overton's conclusion that the lipoids are solely

<sup>6</sup> Proceedings of the Royal Society, 1914, B. 88, p. 320.

<sup>6</sup> Jahrb. f. Wissenschaftl. Botanik, 1900, xxxiv, 669.

<sup>7</sup> Science, March, 1914, xxxix, No. 1003.

<sup>8</sup> Am. Jour. Physiol., 1915, xxxvii.

responsible for the solution of vital stains is untenable. Thionin is insoluble in olive-oil benzol and olive-oil lecithin, but is quite soluble in benzol lecithin; if lecithin were the only factor involved the thionin should go into solution with olive-oil lecithin. He conducted a number of experiments with the eggs of marine animals and many plant cells and root hairs. He found that many acid dyes penetrated various cells. Trypan blue and red, anilin blue and nigrosin penetrate many eggs, and isamin blue, indigo carmin and many other stains penetrate plant cells. The eggs of asterias, unstained by certain dyes, trypan blue and red, were punctured and fluidity gradients formed for the purpose of determining whether the plasma membrane theory were correct. If so a dye which penetrates the surface of a swollen area of cytoplasm ought to penetrate the whole interior of the egg. In the majority of cases the dye did not penetrate the surface of the swollen protoplasm. In no case was the whole interior of the egg stained. Puncture of the cell wall or cell wall and protoplast made most of the plant cells permeable to all the common acid dyes which under the same conditions do not penetrate the unpunctured cells, showing that neither the plasma membrane nor the protoplast but the cell wall is responsible for the impermeability of many plant cells for acid dyes.

In an effort to determine further data relative to the possible relations between the diffusion characteristics of dyes, their solubility in certain substances and their vital staining properties, we performed a large number of experiments. These dyes were studied relative to their diffusion through an animal membrane into water and into various organs which were minced and into which a dialyzing tube containing the solution of the stain was embedded. Their staining reaction in very dilute solutions upon minute particles of various tissues was noted; the permeability of yolk and egg membranes to these dyes was observed and solubility of these dyes in fresh brain tissue tested.

Methylene blue penetrated an animal membrane easily into water, brain and muscle tissue. Minute particles of brain, liver and lung are readily stained in very dilute solutions. It penetrated the membrane of the yolk of a hen's egg readily. The yolk was readily stained. Methylene blue when triturated with the brain of a recently dead fetus apparently was soluble in this tissue.

Trypan blue penetrated an animal membrane hardly at all and very slowly into water—at times not at all into brain tissue, at other times to a degree smaller than into water. It penetrated the yolk membrane but did not stain the yolk. It was insoluble in the brain of a recently dead fetus. Minute particles of brain were unstained in very dilute solutions.

Fluorescein penetrated an animal membrane into water more readily than any of the stains investigated. On one occasion when

employing the brain of a recently dead fetus it did not penetrate into the tissue. Upon all other occasions it did. Minute particles of brain were unstained in very dilute solutions. It penetrated yolk membrane readily, but apparently did not stain the yolk.

Nigrosin and anilin blue penetrated an animal membrane into water readily, but they did not penetrate the membrane of an egg yolk.

Diarscnol penetrated the membrane of an egg yolk.

Such stains as penetrated an animal membrane of a dialyzing tube also penetrated the egg membrane.

From a review of the literature cited above and a study of our experiments certain comments may be made.

Vital stains may possess the characteristic of both crystalloids and colloids. Some vital stains stained all tissues alike. This was especially true of stains possessing great diffusibility, such as methylene blue, etc. However, stains showing a similar degree of diffusibility, as fluorescein, left certain tissues unstained. As a rule the benzidine dyes, possessing colloidal properties, had a selective action, and certain tissues were unstained by them.

If the degree of permeability of certain tissues to stains is solely responsible for the vital staining of organs the bloodvessels and the cell membrane must both be permeated. If we assume that the bloodvessels are responsible in preventing such stains as trypan blue from reaching the brain the theory that their impermeability is dependent upon their lipid character is untenable, because it would have to be assumed that the bloodvessels of the brain possess a different chemical composition from the bloodvessels of other parts of the body. An extra layer of tissue of similar composition, as an extra-adventitial sheath, would not suffice to prevent the escape of the dye if the permeability were governed by physico-chemical laws. The colloid character of dye is probably responsible for failure in penetrating bloodvessels. However, if the colloid character of the dye were solely responsible for its impermeability into the brain, fluorescein should stain the brain easily, which it does not. The experiments of Kite conclusively show that the cell membrane alone is not responsible for absence of *intra vitam* staining. But if it is assumed that the cell membrane is partly responsible for the impermeability of the dye the lipid character of this membrane does not offer a satisfactory explanation for this phenomenon. It would have to be assumed that the cell membranes of the brain, lung and certain other parts of the body differ in composition from the cell membranes elsewhere. The same objections to this view are valid here as they are when applied to vital stains in general. According to this theory the benzidine dyes which are insoluble in fats or lipoids should not stain any tissue *intra vitam*, which is not the case. On the other hand, Salant and Benges<sup>9</sup> found that

<sup>9</sup> Jour. Biol. Chem., November, 1916, No. 2, xxvii, 403.



fat-soluble stains when intravenously introduced were deposited chiefly in the adipose tissue. Only occasionally and under certain circumstances, as starvation, was the nervous system stained. The nerves were stained more frequently than the central nervous system.

Therefore the factors entering into the absence of vital staining of any organ are: Impermeability of the bloodvessel for which the colloid character of the substance may be largely responsible; impermeability of the cell membrane where the lipoid character of such a membrane may play some part and the refusal of the cell content to take up the stain.

Trypan blue probably does not penetrate bloodvessels with the ease and rapidity of methylene blue. It does penetrate bloodvessels, and we cannot assume that the bloodvessels of the brain, lung, portions of the testicle, etc., possess different chemical characteristics from those in other portions of the body. It is a vital stain and penetrates cell membrane, the penetrability not being dependent upon solubility in fats or lipoids. Certain cells refuse to combine with this stain in the living state.

When introduced subdurally in sublethal doses it has been found that the meninges are well stained with trypan blue, and the cord and brain, with which the stain has come in contact, is stained to only a slight depth. When introduced in the lumbar region the stain does not extend over the cerebral hemispheres. When introduced intracranially frequently the opposite side has not been reached by the stain. Woolsey<sup>10</sup> has found that, following sublethal doses introduced subdurally, that the meninges in some areas of the brain were not more stained than by intravenous injections. The brain was not sufficiently stained to be visible microscopically, but the cord was stained from a depth of from 0.5 to 1 mm. True nerve cells were infrequently stained with sublethal doses. Although the brain and spinal cord were stained more readily by subdural than by intravenous administration of trypan blue a study of Woolsey's results did not convince one that the portion of the brain and cord stained were stained *intra vitam* and were uninjured. On the contrary, Woolsey was unable to find any great number of real nerve cells that had taken the stain with sublethal doses. The experiments employing the subdural administration of trypan blue were performed with solutions of a much greater concentration (0.1 to 2 per cent.) than salvarsan solutions used therapeutically.

We have performed experiments on fifteen rabbits and six dogs. We employed subdural injections of dilute solutions of trypan blue and fluorescein, ranging from 0.0025 per cent. to 0.1 per cent. From these experiments it may be stated that trypan blue and fluorescein solutions act similarly under these conditions. Solutions of con-

centration not exceeding that employed in the therapeutic injection of salvarsan subdurally did not stain the brain or spinal cord. Perfusion of trypan-blue solution twice this concentration subdurally over one cerebral hemisphere, allowing the exudate to escape in the lumbar region for a period of an hour, stained the brain a slight sky-blue tint, usually on the side of injection, to a depth which could be removed when the brain was wiped with a bit of wet cotton. With 0.1 per cent. solutions introduced subdurally over one hemisphere the brain substance stained very superficially and faintly on the side of injection over a small area of the occipital lobe, chiefly along the bloodvessels and sulci. Both quadrigeminal bodies, the crurae and the sulci lodging bloodvessels in the cerebellum chiefly on the tentorial side, were superficially stained. The medulla was faintly tinged, the cord was unstained except perhaps in the cervical region, where the stain was hardly perceptible. The meninges of the cord and brain were well stained, except over the side opposite the injection, where the stain was distributed irregularly over the cortex. When the dye was introduced subdurally in the lumbar region, unless injected in large quantities and with enormous force, the cerebral hemispheres were unstained.

Five animals were perfused intravenously with solutions from 0.0025 per cent. to 0.05 per cent., at the same time being bled from the femoral artery. These animals died from five to ten minutes after the blood seemed to have entirely disappeared from the vessel and the muscles were colorless. Under these circumstances the animals injected with 0.05 per cent. showed in the brain a definite change in color, but so slight as to be undefinable. An animal receiving 70 c.c. of a 1 per cent. solution of trypan blue without being bled showed a similar color change in the brain. One animal in which one carotid artery was tied was injected through the opposite carotid with 50 c.c. of 1 per cent. solution of trypan blue. At the end of the time occupied with the injection (five minutes) the animal died. The brain was stained a distinct oyster blue.

Although a slight blue color may be observed macroscopically in cases injected subdurally, microscopic examination has failed to show the presence of a true vital stain. MacCurdy<sup>11</sup> repeated the experiments of Goldmann and found the stain to be an artefact, due to the staining of the fixed tissue by the dye present in considerable concentration.

Although it cannot be proved that such parts of the brain as stain following a subdural injection have changed in viability, it must be assumed that such is the case because the bloodvessels themselves cannot, for the reasons stated above, prevent the penetration of this stain. A substance circulating within bloodvessels through tissues which have no chemical or physical attraction for these substances may be removed too quickly to afford them an

<sup>11</sup> Loc. cit.

opportunity of changing the cell chemistry so that they may penetrate the cell. When applied to these cells in a manner which prevents their rapid removal the cells may undergo a change which permits of their penetration. Any procedure which increases metabolic activity of cells ensures a greater degree of *intra vitam* staining with trypan blue. Whether such an increase, with its attending cell injury as would result from the introduction subdurally of relatively large doses of the stain, or, analogously speaking, large doses of salvarsan are harmless and beneficial, cannot be stated.

It would seem proper to conclude that when dealing with colloidal stains or drugs the meninges are more accessible by subdural than by intravenous routes. This cannot be stated of the central nervous system. When intravenously introduced, certain dyes and salvarsan fail to reach the central nervous system largely because of the physicochemical reactions between the substance and the tissues. The permeability of the bloodvessels plays but a small role and the cerebrospinal fluid and choroid plexus none at all.

Finally, salvarsan, which probably like trypan blue leaks from bloodvessels relatively slowly, when intravenously introduced possesses as great a spirochetocidal action upon those organisms situated in the pia, adventitia and perivascular lesions in the brain as elsewhere, providing the spirochetes have not developed a peculiar resistance to such a drug.

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## THE CIRCULATORY REACTIONS TO GRADUATED WORK IN NORMAL PEOPLE AND IN THOSE WITH CARDIAC INSUFFICIENCY.

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THE important part which physical training plays in the preparation of soldiers for active service and in promoting convalescence from disease or injury makes it desirable to reinvestigate the circulatory reactions following work in both normal people and in those with damaged hearts to see if we can find in these reactions anything which will serve as a guide in estimating the condition of the cardiac reserve power.

We shall first take up the effects of work upon the systolic blood-pressure in normal people. There are two methods of determining the pressure curve after work. In one described by Rapport,<sup>1</sup> readings are taken very frequently (five- to ten-second intervals) by

<sup>1</sup> Arch. Int. Med., 1917, xix, 981.

palpation. In the other method, which we have used for some time, readings are made less frequently by auscultation and at practically equal intervals. Our method is much more convenient, and enables us, as we will shortly show, to construct the curve with sufficient accuracy to achieve our purpose.

For these experiments a sphygmomanometer of the Riva-Rocci type, with a web-covered rubber bulb, was used. The pressure was read by auscultation until it had reached a constant level. The cuff remained on the arm during work and a reservoir of air under pressure was maintained in the rubber bulb. With coöperation on the part of patient and assistant we were generally able to make the first reading, when so desired, as soon as ten seconds had elapsed, and at short intervals thereafter. When using our own method<sup>2</sup> of infrequent readings we made the first reading between twenty-five and thirty seconds after work; the second between fifty-five and sixty; the third between eighty-five and ninety. We endeavored to make the readings as close to thirty, sixty and ninety seconds as was possible.

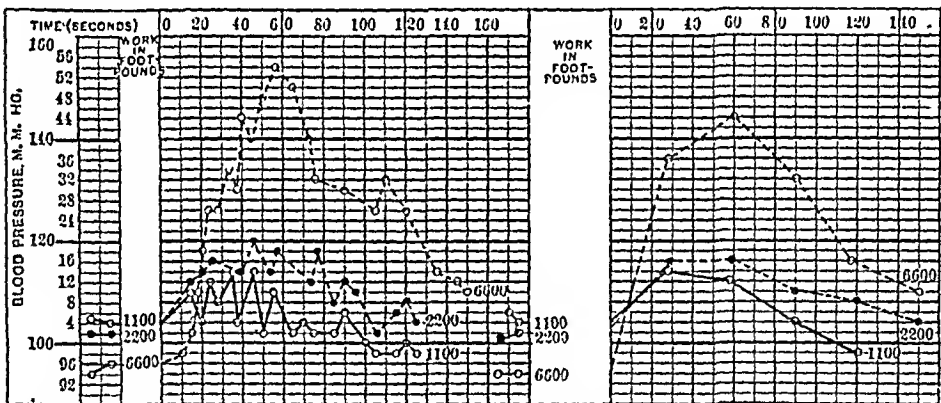


CHART I.—Blood-pressure reactions in a normal man after increasing amounts of work furnished by swinging dumb-bells. Five to ten minutes intervened between the individual exercises. In this and in the succeeding charts the curves on the left were plotted by the frequent method of measurement and on the right by the infrequent method.

We have selected Charts I and II from a number of others as exemplifying the usual reactions following increasing amounts of work in a normal man. The blood-pressure curves are plotted both by the method of frequent reading and by our own method of reading at stated intervals.

The systolic blood-pressure shortly (ten to fifteen seconds) after small or moderate amounts of work is raised; it then mounts rapidly, attaining its summit generally inside of forty seconds and rapidly

<sup>2</sup> In our earlier work the first measurements of the blood-pressure were made between twenty and thirty seconds after work, the second measurement between fifty and sixty seconds after and the third measurements ninety seconds after. The method described in this article undoubtedly gives a more accurate representation of the blood-pressure curve.

subsides. The height of the first readings and of the subsequent rise is dependent, as a rule, on the amount of work and the time in which it is performed.

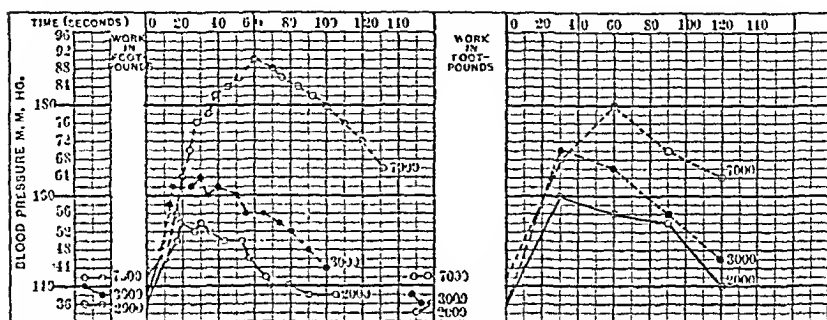


CHART II.—Blood-pressure reactions in a normal man after increasing amounts of work furnished by swinging dumb-bells. Five to ten minutes intervened between the individual exercises.

Following the greatest amounts of work the rise is delayed so that the summit is reached after fifty or more seconds and the subsidence to normal is gradual instead of rapid. This last extreme reaction is what we have termed in our earlier articles a "delayed rise." Cotton, Rapport and Lewis<sup>3</sup> prefer to call this a "delayed summit." The results stated above agree quite closely with their conclusions.

The time at which the pressure reaches its maximum is of considerable importance because it indicates either a rapid or slow development of the blood-pressure curve. In a normal person in good physical training the summit is reached, after all but the heaviest amounts of work, before fifty seconds have elapsed. When the work reaches the limit of effort, judging from the performer's sensations and degree of breathlessness, there ensues a delayed rise, the summit of the pressure falling somewhere between fifty and ninety seconds, and the curve then slowly subsides to normal.

The term "delayed rise" will be used, therefore, to indicate that form of the systolic blood-pressure curve which shows a delayed rise, with a summit occurring between fifty and ninety seconds after work. It presents no qualitative difference from the curves following moderate amounts of work, but is simply an exaggeration of what might be called the "normal type." An examination of the curves obtained by the infrequent method of measurement (see Chart I) shows that a delayed rise, with all that it implies as to the form of the pressure curve, will be revealed by this much simpler method with almost as much certainty as by Rapport's method.

This circulatory reaction possesses, we believe, peculiar significance, and we will enumerate the facts we have discovered about the delayed rise following work in normal people.

*The Delayed Rise in Normal People.* (a) In a normal person in good physical training a delayed rise is found only after heavy work, and is accompanied by marked breathlessness. The limit of effort is apparently approached when this reaction ensues.

The amounts of work which delay the summit to between fifty and ninety seconds vary for different persons according to their condition of physical training.

We have never failed to elicit a delayed rise in normal people at some stage as they performed progressively increasing quantities of work.

(b) A normal person in poor physical training will show a delayed rise after moderate amounts of work which are not accompanied by as marked breathlessness as is noted under (a).

(c) The production of a delayed rise is dependent on the amount of work and the time in which it is performed (power expended) and not on the group of muscles employed.<sup>4</sup>

(d) The amount of work which is followed by a delayed rise varies but little from day to day. Chart III exemplifies this.

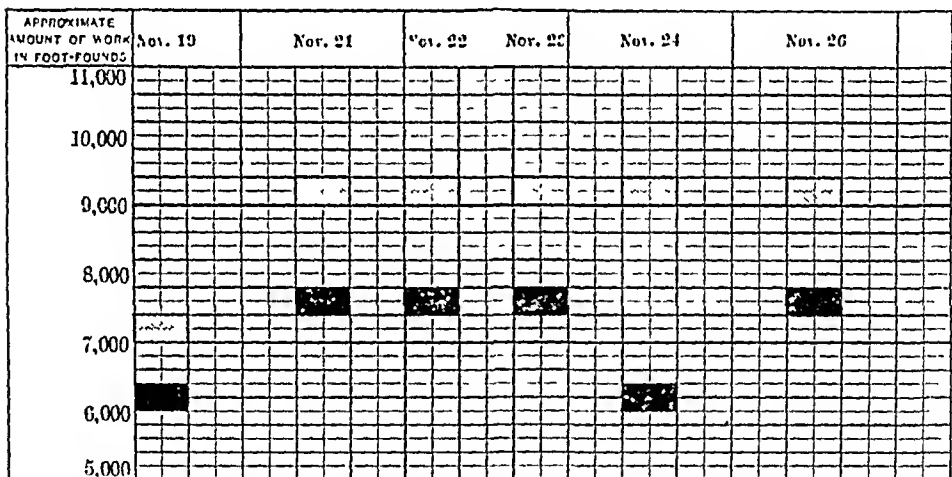


CHART III.—Daily variations in amounts of work performed by normal persons which were followed by delayed rises. The black squares represent work which was not followed by a delayed rise. Shaded squares represent work which was followed by a delayed rise.

(e) Children are able to perform relatively larger amounts of work without producing a delayed rise than are adults, taking into consideration their respective weights.<sup>5</sup> After thirty years of age the amounts of work which can be performed without evoking delayed rises gradually decrease.

(f) Physical training increases rapidly the amounts of work which can be performed without delayed rises ensuing.

<sup>4</sup> Arch. Int. Med., 1916, xvii, 366. Although not so stated, all first measurements in this article were made between twenty and thirty seconds after work.

<sup>5</sup> Personal communication, Dr. W. P. St. Lawrence.

(g) During convalescence from infectious diseases the amounts of work which can be performed without delayed rises are small at first and then increase rapidly.<sup>6</sup>

*The Systolic Blood-pressure after Work in Patients Suffering from Marked Cardiac Insufficiency.* Two patients with rhythmical pulses were selected whose cardiac reserve powers were obviously exhausted and their curves after work were plotted by both the frequent and the infrequent methods of reading the blood-pressure.

The first patient, M. W., aged twenty-one years, was suffering from an old rheumatic endocarditis which had left him with a double mitral and an aortic lesion. As he lay in bed he was dyspneic, his legs were swollen, the liver was enlarged and there were many moist rales at the base of the lungs.

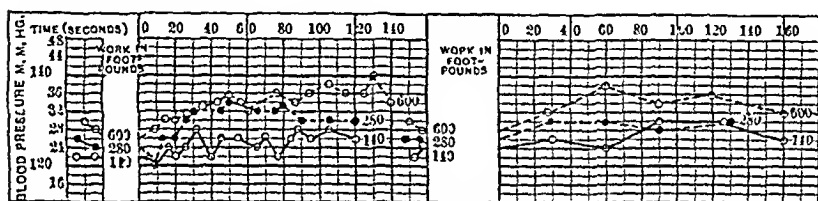


CHART IV.—Blood-pressure reactions after increasing amounts of work furnished by flexing dumb-bells in patient M. W., suffering from extreme cardiac insufficiency (reserve power = 0).

The second patient, L. G., aged seventeen years, was suffering from cardiac insufficiency following a rheumatic lesion of the mitral and aortic valves. He was dyspneic as he sat in a chair, both lungs showed moist rales at the bases and his liver was enlarged. He had no pretibial edema. Chart V shows his blood-pressure reactions.

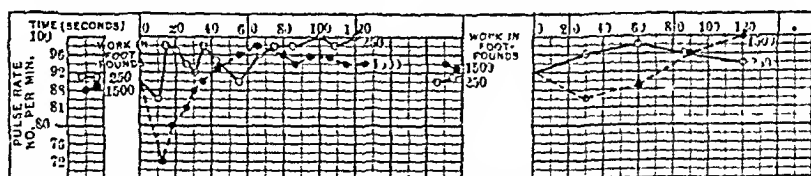


CHART V.—Blood-pressure reactions after increasing amounts of work furnished by dumb-bell movements in patient L. G., suffering from marked cardiac insufficiency (reserve power = 0).

The blood-pressure curves in these charts are quite typical of the curves we have obtained in all patients suffering from grave cardiac insufficiency. The first reading is often below that noted before work. As the work is increased the first reading frequently falls lower and lower. This peculiarity is also often observed when we use the infrequent method of plotting the curve. The development of the curve is greatly prolonged, as is evidenced by the marked delay

\* Personal communication, Dr. Hubert Mann.

in the rise. The amounts of work which produce this curve are very small as compared with those in normal subjects. Chart V shows very well the effect of a marked increase in work. Instead of mounting higher, as it would in a normal person, the initial drop of the blood-pressure was simply accentuated. The curve otherwise greatly resembles that following the much smaller amount of work.

The similarity between these curves, obtained in patients with no cardiac reserve power, and the curves with a delayed rise in normal people, is marked and affords a valuable clue to the significance of this type of blood-pressure curve.

*The Systolic Blood-pressure after Work in Patients Suffering from Moderate Cardiac Insufficiency.* The patient whose curves are represented in Chart VI was selected as a typical example of this class of patients. She was an ambulatory patient with mitral stenosis arising from rheumatic endocarditis. She was able to walk on the level slowly without discomfort. Going up one flight of stairs (twenty steps) caused marked breathlessness and palpitation, obliging her to stop and rest after ten steps. She had no edema of the legs or lungs.

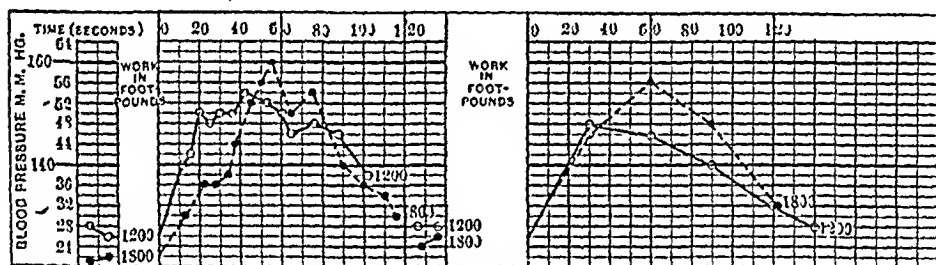


CHART VI.—Blood-pressure reactions in a patient with moderate cardiac insufficiency after increasing amounts of work furnished by dumb-bell movements. Five to ten minutes intervened between the individual exercises.

It will be noted that 1800 foot-pounds of work was followed by a delayed rise and was accompanied by marked dyspnea and palpitation. She was able to perform 1200 foot-pounds without causing a delayed rise and with but moderate breathlessness.

*Improvement in Cardiac Insufficiency and its Effect upon the Delayed Rise.* Patients suffering from varying degrees of cardiac insufficiency show, as they improve, a steady increase in the amounts of work they are able to perform without causing this reaction. Chart VII exemplifies the foregoing statement.

*The Significance of the Delayed Rise in Systolic Blood-pressure.* The primary meaning of this reaction is that the curve of the systolic blood-pressure, if plotted out, would have the form described and depicted in the first part of this article.

In order to appreciate the significance of this form of the blood-pressure curve the facts we have enumerated about this reaction in normal people must be considered. Of these the most important



are the invariability of the delayed rise after a stated amount of work performed in a stated time quite irrespective of the group of muscles

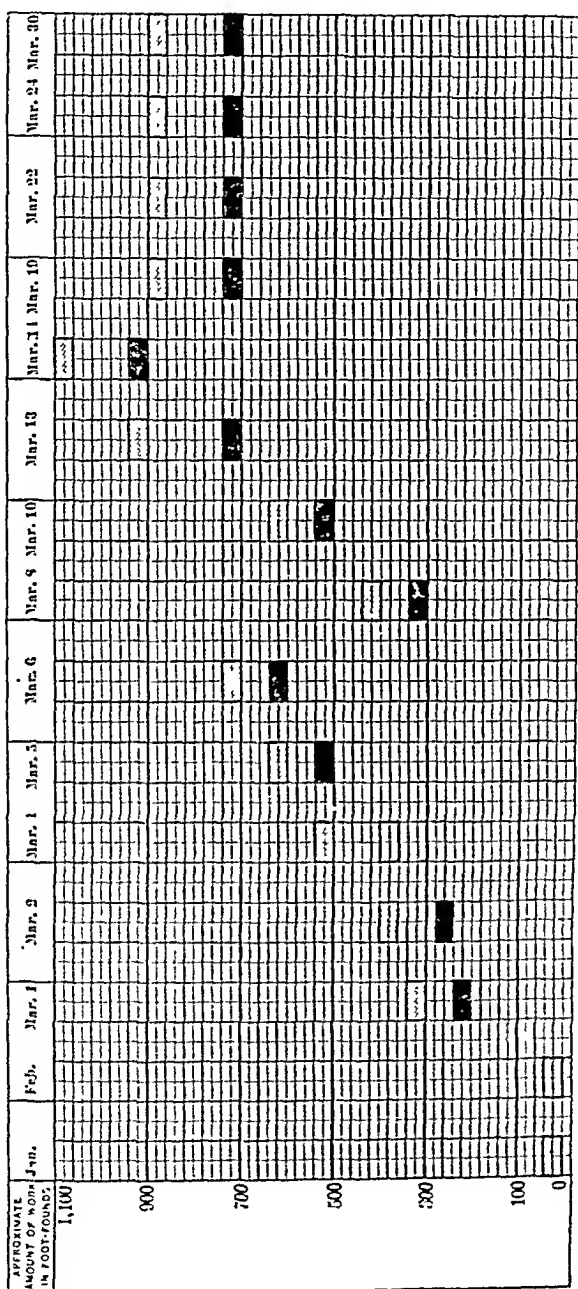


CHART VII.—The increase in the amounts of work performed by the patient G. C. which were not followed by delayed rises. This patient at the outset suffered for one month from extreme cardiac insufficiency, and, coincident with the increase, his clinical condition improved markedly. The black squares represent work which was not followed by a delayed rise; the shaded squares, work which was. The empty squares indicate that any work whatsoever was followed by a blood-pressure curve similar to those in Charts IV and V.

employed; the small variations from day to day of the quantities of work which cause this reaction; the relatively greater amounts of

work which children, as compared to adults, can perform, taking their respective weights into consideration, before this reaction ensues; and the marked effect which physical training has in increasing the amounts of work a person can accomplish without evoking a delayed rise.

It is the type of curve obtained after minimal amounts of work in patients with no cardiac reserve power, however, which does most to make clear the meaning of this reaction in healthy people. These curves always show a delayed rise with a very slow return to normal, and are quite similar to the curves initiated by a delayed rise in normal persons.

TABLE I.—PULSE REACTIONS IN NORMAL MEN.

Patient.	Work.	Pulse rate.		Return to normal, seconds.	Delayed rise, systolic pressure.	Delay, seconds.
		Before.	Immediately after.			
J. M., aged twenty-four years.	20 S. 5	96	112	120	No	
	20 S. 10	72	118	180	No	
	30 S. 10	80	120	180	Yes	58
	20 S. 20	88	128	240	Yes	60
	20 S. 30	88	140	300	Yes	60
A. Q., aged twenty-six years.	15 S. 10	72	104	120	No	
	15 S. 15	72	108	118	Yes	60
	15 S. 20	70	104	120	No	
	20 S. 20	88	128	120	Yes	60
	30 S. 20	68	124	300	Yes	60
	30 S. 20	68	112	120	No	
	30 S. 25	72	128	120	No	
	30 S. 30	84	112	180	Yes	60
	30 S. 20	84	112	180	No	
	30 S. 25	88	136	120	Yes	60
	30 S. 35	88	136	240	Yes	60
R. O., aged twenty-three years.	20 S. 10	104	128	120	No	
	20 S. 15	104	140	180	No	
	20 S. 25	104	158	180	Yes	60
	20 S. 35	104	156	240	Yes	60
W. M., aged twenty-two years.	20 S. 15	90	112	180	No	
	20 S. 20	96	128	120	Yes	60
	20 S. 25	96	124	120	Yes	60
R. T., aged forty-one years.	20 S. 30	88	120	150	No	
	20 S. 35	84	136	240	No	
	20 S. 40	84	140	300	No	
	20 S. 45	84	148	360	Yes	60

The effect of work upon the pulse rate of normal men. There was a period of from five to ten minutes between the individual exercises. The figures 120 in the column headed "Return to Normal" means that the rate became normal after two minutes or earlier.

Another fact which has an important bearing on this question is that, coincident with the improvement of patients suffering from cardiac insufficiency, there occurs an increase in the amounts of work they can perform without producing delayed rises.

There is but one conclusion, it seems to us, which can be drawn

from these facts, and that is that a delayed rise of systolic blood-pressure, with all that it implies as to the form of the pressure curve, means that the preceding work has either overtaxed or is on the point of overtaking the heart's reserve power. If this conclusion is correct it is a simple matter to use comparisons of the amounts of work causing the delayed rise as an indirect measure of the cardiac reserve power.

TABLE II.—PULSE REACTIONS IN PATIENTS WITH CARDIAC INSUFFICIENCY.

Patient.	Work in foot pounds.	Pulse rate.		Return to normal, seconds.	Delayed rise, systolic pressure.	Delay, seconds.
		Before.	Immediately after.			
J.S., aged twenty-seven years. Marked cardiac insufficiency.	200	100	116	180	Yes	90
	200	116	124	120	Yes	120
	300	112	120	120	Yes	120
	300	120	128	120	Yes	88
M. W., aged twenty-seven years. Marked cardiac insufficiency. Reserve power zero.	60	104	108	120	Yes	60
	140	108	116	180	Yes	90
	280	112	112	120	No	
	400	112	116	120.	Yes	120
	400	106	112	120	Yes	88
	450	112	120	180	Yes	120
	140	108	116	125	Yes	90
	280	106	118	120	Yes	85
	600	112	118	120	Yes	60
	140	108	110	120	No	
	200	108	114	120	Yes	58
	200	108	118	120	Yes	90
	600	84	104	120	Yes	90
	1200	88	112	120	Yes	90
	250	66	80	120	No	
L. G., aged seventeen years. Moderate insufficiency.	375	64	76	120	Yes	90
	500	64	80	120	Yes	90
	750	68	88	120	Yes	58
	1200	76	108	120	Yes	88
	250	84	88	120	Yes	60
	500	72	80	120	Yes	60
	750	76	104	180	Yes	60
	200	72	100	120	No	
	500	76	100	180	No	
	750	80	100	120	Yes	90
	1200	78	118	118	Yes	88
	2000	78	132	240	Yes	90
	250	90	102	120	Yes	60
	900	90	112	300	Yes	118
	1400	92	128	180	Yes	120
S. T., aged fifty-eight years. Moderate cardiac insufficiency.	700	76	88	120	No	
	2000	74	96	120	Yes	90
E. C., aged thirty-four years. Moderate cardiac insufficiency.	170	92	108	120	No	
	340	88	80	...	No	
	1100	84	104	120	No	
	2000	80	...	180	Yes	60

The effect of work upon the pulse rate of patients suffering from varying degrees of cardiac insufficiency. Five to ten minutes intervened between the individual exercises. The figure 120 in the column headed "Return to Normal" means that the rate became normal after two minutes or earlier.

*The Effect of Work upon the Pulse Rate in Normal Individuals.* It has been our experience that changes in pulse rate following work have seldom afforded any reliable indication as to the condition of the heart's reserve power. Recently, Mekins and Gunson<sup>7</sup> have published their investigations upon the effect of exercise on the pulse rate in patients suffering from "disordered action of the heart." One of their conclusions was that patients in whom the pulse rate did not return to normal within a short period of time (*i. e.*, two minutes) performed the simplest exercises with difficulty. With this particular conclusion in mind we have observed the pulse rate after work in a few normal people and in a few patients with cardiac insufficiency.

The pulse was counted before exercise and then for fifteen seconds immediately after exercise. At the end of one hundred and ten seconds it was then counted again for twenty seconds. From these counts the rates per minute immediately after work and at the end of one hundred and twenty seconds were calculated. If the rate at the end of two minutes was within six beats of the pre-exercise rate it was considered to have returned to normal. Table I summarizes our results in normal people.

There were 27 experiments carried out on five normal men. A delayed rise of the systolic pressure occurred fourteen times and was accompanied nine times by a pulse rate which did not return to normal inside of two minutes. Thirteen times there was no delayed rise, and yet on seven occasions the pulse rate did not return to normal inside of two minutes.

*The Effect of Work upon the Pulse Rates of Patients Suffering from Varying Degrees of Cardiac Insufficiency.* Table II summarizes our results in patients who had either a moderate or no cardiac reserve power.

There were 40 experiments carried out on 5 patients. A delayed rise of the systolic pressure occurred 31 times and was accompanied 9 times by a pulse rate which did not return to normal inside of two minutes. Twenty-two times the pulse rate returned to normal two minutes or sooner after work.

The results of these experiments, carried out on normal persons and those suffering from cardiac insufficiency, few in number though they are, tend to confirm our belief that the time required for the pulse rate to return to normal affords but little information, in either normal people or patients with cardiac insufficiency, as to the condition of the heart's reserve power.

CONCLUSIONS. The occurrence of a delayed rise in systolic blood-pressure after work indicates that the preceding work has either overtaxed or is on the point of overtaking the heart's reserve power. The presence of a delayed rise can be determined by the

<sup>7</sup> Heart, 1917, vi, 285.

infrequent method of plotting the pressure curve with almost as much certainty as by the frequent method.

A small number of experiments upon normal people and upon patients with cardiac insufficiency showed that no definite relation existed between the time required for the pulse rate to return to normal and the condition of the cardiac reserve power.

We wish to express our thanks to Dr. William R. Williams, whose hospital service furnished the material for the foregoing work, for his advice and coöperation in carrying out the same.

## PERFORATED GASTRIC AND DUODENAL ULCER: A STATISTICAL REPORT OF FIFTY-NINE CASES.

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(From the Clinics of the Cook County Hospital.)

DURING the last six years (1911 to 1916 inclusive) there were 59 cases of perforated gastric and duodenal ulcer admitted to the Cook County Hospital. Of these cases 48 were perforated gastric ulcers and 11 perforated duodenal ulcers. During this same period the total number of ulcer cases was 506 gastric ulcers and 72 duodenal ulcers. The frequency of perforation in these cases was 9.4 per cent. in gastric ulcer and 15 per cent. in duodenal ulcer. The patients were seen at varying periods of time after the perforation, some shortly after while others were moribund and in shock. Only those cases in which the perforated ulcer was seen at operation or at autopsy are included in this series. All cases of doubtful diagnosis have been excluded in order to make the data more accurate. Forty-nine of the patients were operated upon by ten different staff surgeons. In the remaining 10 cases the ulcer was recognized at autopsy.

*Age and Sex Incidence.* Of the perforated gastric ulcers 44 were in males and 4 in females. Caird<sup>1</sup> in a series of 247 cases from the Edinburgh Hospital found a greater percentage of perforated gastric ulcers in females. Connors<sup>2</sup> in a series of 41 cases found 36 in males and 5 in females. The perforated duodenal ulcers were all in males. This agrees with the findings of Caird,<sup>3</sup> who reported 179 males and 21 females in a series of 200 cases.

The majority of the perforations occurred between the ages of thirty and forty years in gastric ulcer and between twenty and thirty years in duodenal ulcer, as will be noted in the following table:

Age.	Gastric ulcer.	Duodenal ulcer.
Under 20 years . . . . .	1 cases	0 cases
20 to 30 " . . . . .	12 "	7 "
30 to 40 " . . . . .	19 "	2 "
40 to 50 " . . . . .	9 "	2 "
50 to 60 " . . . . .	4 "	0 "
60 to 70 " . . . . .	3 "	0 "

The occupation of the patient did not seem to have any bearing, as many trades were represented, and none that would seem at all a predisposing factor.

*Previous Gastric Disturbance.* It is difficult to obtain an accurate history of any previous stomach trouble when the patients are first seen, due to their acute suffering. The majority, however, recall some previous gastric disturbance. In this series, 29 cases of gastric and 6 cases of duodenal ulcer gave a history of previous trouble of variable duration.

Duration.	Gastric ulcer.	Duodenal ulcer.
Under 1 year . . . . .	5 cases	2 cases
1 to 5 " . . . . .	11 "	4 "
5 to 20 " . . . . .	3 "	0 "
No duration noted . . . . .	10 "	0 "

Sixteen cases of perforated gastric and 5 cases of duodenal ulcer gave no history of previous gastric disturbance. This may not be a true statement, as the patient's condition was often extremely grave, and the history consequently was rather hurriedly and briefly obtained. Often the patient agreed to any question asked, so that many contradictory facts were obtained. Oftentimes slight stomach complaints, as heartburn or slight discomfort after meals, were never thought of by the patient when asked if he had any previous stomach trouble, and were elicited only on careful inquiry. However, it is true that there may be an entire absence of any antecedent indigestion and the perforation may occur without warning.

*Premonitory Symptoms.* There are no characteristic prodromal symptoms which may give warning that perforation is about to occur. In several cases it was noted that the symptoms of indigestion were worse than usual for several days preceding the perforation, but such exacerbations are not infrequently experienced in gastric disorders apart from perforation. Many cases gave no prodromal symptoms whatever. In this series 27 cases of gastric and 2 cases of duodenal ulcer gave variable prodromal symptoms. The most constant symptom was pain, usually slight, located in the upper abdomen, and in some cases associated with food taking. Vomiting occurred in several cases. Two cases gave a history of alcoholic excesses previous to the perforation.

*Determining Cause.* No single factor can be assigned as being the determining cause of the rupture. In 7 cases the perforation occurred while doing heavy work. It is conceivable that severe muscular effort might have determined the actual rupture of an ulcer, the base of which was already weakened. In several cases perforation occurred shortly after eating, but in a considerable proportion of the cases it occurred from six to ten hours after food was taken, so that the entrance of food into the stomach did not always appear to have a determining influence.

*Onset.* In practically every case the onset was sudden, with agonizing pain in the epigastrium, often doubling up the patient on account of the extreme severity. Brunner<sup>4</sup> in a series of 263 cases of gastric and 52 cases of duodenal ulcer reported there was an acute onset of pain in 260 of the gastric ulcer cases and in 49 of the duodenal ulcer cases. In a great majority of the cases the pain was located in the epigastrium. In gastric ulcer the point of maximum intensity was generally a little to the left of the midline, while in duodenal ulcer it was a little to the right. In a few cases the pain was generalized or was localized in the lower abdomen.

Location of pain.	Gastric ulcer.	Duodenal ulcer.
Epigastrium . . . . .	37 cases	9 cases
Generalized . . . . .	3 "	2 "
Lower right side . . . . .	3 "	0 "
Lower left side . . . . .	1 "	0 "

Vomiting occurred in 35 cases of perforated gastric ulcer shortly after perforation and in 6 cases of duodenal ulcer. Several patients were nauseated, but did not vomit.

*Period of Reaction.* Following the sudden onset of pain there is a period of remission coming on from two or three hours after the perforation. This was noted in a large proportion of the cases. The acute symptoms abate and the patient looks and feels better. The physician called in at this time may not recognize the seriousness of the condition and delays sending the patient to a hospital. The recurrence of pain indicates the onset of peritonitis. Kennedy<sup>5</sup> recognizes three periods following perforation: (1) the stage of shock and collapse; (2) the stage of reaction; (3) the stage of diffuse peritonitis. It is during the second stage or the period of remission that the diagnosis is most difficult, but a mistake may not be serious if the patient is operated upon at once and the true condition recognized.

*Findings.* Many patients were not seen until some time after perforation had occurred. Eight cases of gastric and 2 cases of duodenal ulcer were moribund on entrance. In the majority of cases seen early the point of maximum tenderness corresponded closely to the point of maximum pain. In late cases the tenderness was generalized.

Location of tenderness.	Gastric ulcer.	Duodenal ulcer.
Epigastrium . . . . .	24 cases	5 cases
Generalized . . . . .	23 "	5 "
Right lower . . . . .	1 "	1 "

Rigidity was present in practically every case, though of varying degree, and was especially marked in the upper abdomen. Tympanites was noted in 16 cases of gastric and in 6 cases of duodenal ulcer. Fluid was diagnosed in 14 cases of gastric and in 6 cases of

duodenal ulcer. Schoemaker<sup>6</sup> has pointed out that in percussing fluid in the flank an increase of pressure on the percussed finger displaces the fluid, bringing the intestines closer, and thus a tympanitic note is elicited. As a result small amounts of fluid may be overlooked. Thirteen cases of gastric ulcer were in shock on entrance, with rapid pulse, pallor and a subnormal temperature. Few cases showed a febrile reaction; these were late cases with a generalized peritonitis. The pulse and leukocytes are given in the following table:

Duration of perforation.	Cases recovering.		Cases fatal.	
	Pulse.	Leukocytes.	Pulse.	Leukocytes.
Under 5 hours . . .	86	13,600		
5 to 15 " . . .	108	13,300	128	10,100
15 to 24 " . . .	80	15,600	106	20,000
Over 24 " . . .	98	17,900	112	18,600

In early stages the pulse was not much increased in rate, though there was a moderate increase in the leukocyte count. In later stages the pulse became more rapid and the leukocytes increased slightly. It is worthy of note that in the cases recovering the pulse was never as rapid as in the cases which resulted fatally. This was probably due to a more virulent peritonitis and a greater degree of shock in those cases. Petrén<sup>7</sup> noted that the pulse was slower in the early stages and that the percentage of mortality was less in cases with a slow pulse. This will be noted in the following table from his report:

		Pulse frequency.	
1 to 5 hours . . . . .		80 to 100 per minute	
5 to 10 " . . . . .		90 to 110 "	
10 to 15 " . . . . .		110 to 120 "	
		Pulse rate.	Recovery.
21 cases . . . . .		80 to 100	16 cases
7 " . . . . .		104 to 120	5 "
2 " . . . . .		125 to 140	0 "
			Death.
			5 cases
			2 "
			2 "

Certain early cases had a high leukocyte count with a pulse below 90. Finney<sup>8</sup> considered a leukocytosis in a young person with a history of previous gastric disturbance as a diagnostic sign of considerable importance.

*Diagnosis.* The diagnosis made before operation in this series of cases is noted in the following table:

Diagnosis.	Gastric ulcer 48 cases.	Duodenal ulcer 11 cases.
Perforated gastric ulcer . . . . .	21 times	3 times
Perforated duodenal ulcer . . . . .	2 "	1 "
Acute appendicitis . . . . .	6 "	3 "
Acute cholecystitis . . . . .	3 "	0 "
Acute abdomen (peritonitis) . . . . .	13 "	4 "
Ileus . . . . .	2 "	0 "
Liver abscess . . . . .	1 "	0 "

The diagnosis was not difficult when the case was seen early and a good history obtained. The conditions with which perforation was



most frequently confused were, in the early-stages, acute appendicitis, acute cholecystitis and acute pancreatitis, and in the late stages ruptured appendix and general peritonitis from an unrecognized source. The absence of a febrile reaction in the early stages and the history of a sudden, agonizing pain helped to differentiate from other acute abdominal conditions.

In appendicitis the onset of the pain is more gradual, its location is in the lower right side and it is preceded by a rise in temperature. Acute cholecystitis is more difficult to distinguish, though the pain is located somewhat farther out from the midline. Acute pancreatitis is relatively infrequent and is therefore rarely confused.

In several of the cases an incision was made for an appendectomy, and only upon opening the abdomen was the perforation recognized. In a perforated ulcer the fluid is uniform and is usually more abundant as the upper abdomen is exposed, while in appendicitis the fluid becomes thicker and more purulent as the appendix is approached. The appendix itself presents greater gross changes.

In the late cases, when the tenderness and rigidity were generalized, a correct diagnosis was made, as a rule, only upon exploratory incision. A history of previous gastric disturbance and the location of the pain in the epigastrium at the onset helped to place the source of the peritonitis in the upper abdomen. Methylene blue<sup>9</sup> was given by mouth in several cases of suspected perforation before operation, and the finding of stained free fluid upon opening the abdomen confirmed the diagnosis.

*Operation.* An operation was performed in 40 cases of gastric and in 9 cases of duodenal ulcer. Many were in late stages and in shock when operated, and survived for only a short time. The remaining 10 patients were in such serious condition when seen that no operative procedure was thought advisable.

*Fluid.* As a rule the peritoneal cavity contained a variable amount of fluid. It was present in 37 cases of gastric and in 9 cases of duodenal ulcer. The character varied with the duration of the perforation. In early cases it was serous and at times bile-stained. In late cases it was thicker and seropurulent. Free stomach contents were noted in 10 cases of gastric and in 3 cases of duodenal ulcer. In 2 cases of perforation through the posterior wall of the stomach the fluid was limited to the lesser peritoneal cavity. In 1 case the fluid was purulent and limited by dense adhesions about the duodenum.

Associated with the fluid was a peritonitis of varying grades, depending upon the duration of the perforation. In early cases the surface was reddened and inflamed, while in late cases it was covered with a fibrinous exudate.

*Site of Perforation.* The most common site of perforation in gastric ulcers is on the anterior wall of the stomach near the pylorus along the lesser curvature. The perforation was anterior, near the pylorus in 43 cases, anterior in cardia in 1 case, and posterior in 4

cases. Multiple perforating ulcers were noted in 2 cases. The perforating ulcer of the cardia was associated with a carcinoma of the stomach wall. Caird<sup>1</sup> in 228 cases found the perforation on the anterior wall in 209 cases and on the posterior wall in 19 cases. In all cases recovering after operation the ulcer was located anterior near the pylorus. All cases on the posterior wall resulted fatally. Induration was present about the ulcer in practically every case.

In all the cases of duodenal ulcer the perforation was anterior in the first portion near the pylorus. Multiple ulcers were present in one case, but only one was perforated. Caird<sup>3</sup> in 118 cases noted the perforation on the anterior surface in 101 cases, on the superior surface in 13 cases and on the posterior surface in 4 cases. The size of the perforation in both gastric and duodenal ulcer was variable. The larger ones were generally more fatal.

*Procedure.* In the majority of cases a simple closure of the perforation by Lembert suture and drainage was done. Other procedures were employed in a few cases.

Procedure. Gastric ulcer.	Cases.	Recovery.	Death.
Closure and drainage . . . . .	26	12	14
Closure and gastro-enterostomy . . . . .	5	4	1
Excision and suture . . . . .	1	0	1
Drainage, not closed . . . . .	5	0	5
Closure, no drainage . . . . .	1	0	1
Gastrostomy . . . . .	1	0	1
No operative record . . . . .	1	0	1
Duodenal ulcer.			
Closure and drainage . . . . .	5	4	1
Closure and gastro-enterostomy . . . . .	3	1	2
Drainage, not closed . . . . .	1	0	1

In 5 cases of gastric and in 1 case of duodenal ulcer simple drainage was done, as the patient's condition was so grave that no further procedure was deemed advisable; all resulted fatally. In 1 case a rubber tube was inserted into the stomach through the perforation, and in 5 cases of gastric and in 3 cases of duodenal ulcer a primary gastro-enterostomy was done in addition to closure of the perforation, with 5 recoveries. The advisability of doing a routine gastro-enterostomy at the time of repair of the perforation has been widely discussed. Eliot<sup>10</sup> has given an excellent review of this subject, and is of the opinion that a gastro-enterostomy is indicated only when the lesion itself is of such an extent that its suture or subsequent cicatricial deformity would lead to a persistence or recurrence of symptoms.

*Immediate Results.* Of the 40 cases of perforated gastric ulcer operated upon 16 recovered and 24 died, and of the 9 cases of duodenal ulcer 5 recovered and 4 died. Many patients died in shock within the first twenty-four hours following the operation. Others continued weak for days afterward and finally succumbed to general peritonitis. The cause of death and complications in the operated cases are given in the following table:

*Cause of Death. Gastric Ulcer (24 cases).*

Eighteen cases with closure of perforation.

2 cases died under anesthetic.

7 cases died in shock within twenty-four hours.

6 cases died of generalized peritonitis.

1 case died of subphrenic abscess.

1 case died after partial closure of ulcer.

1 case died after perforation of second ulcer.

Six cases with no closure.

1 case died in shock in twenty-four hours.

1 case had carcinoma of cardia also.

1 case developed peritonitis after gastrostomy.

3 cases developed general peritonitis, all posterior ulcers.

*Duodenal Ulcer (4 cases).*

2 cases died in shock in eighteen hours.

2 cases died of general peritonitis.

*Hours Elapsing after Perforation until Operation.* The patients were operated upon at different periods of time after perforation, and it will be seen from the following table that those operated within the first twelve hours had a greater percentage of recoveries:

Gastric ulcer.		Cases.	Recovery.	Death.
Under 5 hours	. . . . .	4	4	0
5 to 15 "	. . . . .	13	7	6
15 to 24 "	. . . . .	9	2	7
Over 24 "	. . . . .	14	3	11
Duodenal ulcer.				
Under 5 hours	. . . . .	1	1	0
5 to 12 "	. . . . .	2	1	1
12 to 24 "	. . . . .	3	2	1
Over 24 "	. . . . .	3	1	2

*Mortality.* The mortality of the operated cases was 60 per cent. in gastric ulcer cases and 44.4 per cent. in duodenal ulcer cases. The mortality, including cases not operated upon, was 66.6 per cent. in gastric ulcer cases and 55.5 per cent. in duodenal ulcer cases. Caird<sup>13</sup> gave the mortality as 42.5 per cent. in 247 cases of gastric ulcer and as 39.5 per cent. in 200 cases of duodenal ulcer. Collinson<sup>11</sup> gave the mortality as 53.8 per cent. in 13 cases of gastric ulcer and as 32.5 per cent. in 40 cases of duodenal ulcer. The mortality is directly proportionate to the length of time elapsing after the perforation.

Mortality.		Gastric.	Duodenal.
Cases operated upon under 5 hours	. . .	0.0 per cent.	0.0 per cent.
" " " 5 to 15 "	. . .	46.1 "	50.0 "
" " " 15 to 24 "	. . .	77.0 "	33.3 "
" " " over 24 "	. . .	78.5 "	66.6 "

The fact that cases operated upon after twenty-four hours do recover is due to the localizing of the infection. Walker<sup>12</sup> in 78 cases gave the mortality of cases operated upon in from five to twelve hours as 17.9 per cent.; twelve to twenty-four hours as 46.6 per cent., and over twenty-four hours as 66.2 per cent. Connors<sup>2</sup> in

42 cases gave the mortality as 20 per cent. in cases operated upon under six hours and as 66 per cent. in cases over six hours.

In 16 cases of gastric ulcer which recovered after operation, 11, or 68.7 per cent., were operated upon within fifteen hours after perforation had occurred. In the 24 cases which resulted fatally only 6, or 25 per cent., were operated upon within fifteen hours. This is similar to the findings of Caird<sup>1</sup> in his series of cases. In cases which recovered 65.9 per cent. were operated upon within twelve hours, while in cases which were fatal only 34.6 per cent. were operated upon in that time.

In 5 cases of duodenal ulcer which recovered, 3, or 60 per cent., were operated upon in the first twelve hours, while in the 4 cases resulting fatally only 1, or 25 per cent., was operated upon in the first twelve hours. Caird<sup>3</sup> in a series of 200 cases found that in the cases which recovered 73.1 per cent. were operated upon in the first twelve hours, while in the cases which resulted fatally only 37.6 per cent. were operated upon in that time.

COMMENT. From a study of these cases it becomes evident that an early recognition of the condition followed by an immediate operation is necessary for the best results. This is well illustrated by the fact that all cases diagnosed and operated upon within the first five hours recovered, while in those operated later there was a mortality proportionate to the delay. The diagnosis should be made when the patient is first seen if possible and immediate operation insisted upon. The difficulty in diagnosis is due to the period of reaction that follows the acute onset, during which time the patient appears so much better that the seriousness of the condition is overlooked. This point cannot be too strongly emphasized, as a large proportion of the delayed cases entering the hospital are due to the mistaken opinion of the attending physician. The diagnosis is too often that of a mild colic which is expected to pass away in time, but instead symptoms of peritonitis develop, and only then is the seriousness of the condition recognized. Even in delayed cases an operation should be performed, for otherwise the result is almost invariably fatal.

Considerable confusion in the diagnosis of perforation arises from the fact that the patient presents a markedly different clinical picture in the various stages. The symptoms are not progressive and the physical signs are not well developed until comparatively late.

At the onset, during the stage of shock, the patient is pale and faint, with an anxious expression on the face, and holds the body absolutely rigid on account of the intense abdominal pain. The marked severity of the pain is thought by some to be due to the chemical irritation of the peritoneum by the escaping stomach contents. The abdominal wall is retracted and so extremely rigid that very little can be determined on examination. The breathing is short and quick, and is of the costal type. Vomiting may be present, but is not of much significance, as it may be absent in per-

foration and present in so many other conditions. The leukocyte count is normal or may be slightly increased; the temperature is usually normal or may be subnormal. Perforation should not be ruled out because of a slow pulse and a normal temperature, or because of a normal or an increased leukocyte count, as these are frequent findings in this stage.

Following the acute onset there may be a period of remission during which the patient feels much better. The patient relaxes and breathing is much easier. The abdomen is less rigid, though there is a local rigidity in the upper abdomen and a tenderness confined to the region of the perforation. On careful examination fluid may be demonstrated in the flank, which is a very valuable sign. The pulse is still slow but gradually increases in frequency. The temperature also rises slightly. Diagnosis in this stage depends largely on the history of the onset. An acute attack of violent abdominal pain associated with shock and followed by a period of improvement is always significant.

Finally the symptoms of peritonitis become evident. The patient is restless, with sunken eyes and a drawn, facial expression. The abdomen becomes distended and the liver dulness is diminished. Fluid is not so easily demonstrated. The pain and tenderness are generalized and the rigidity is now board-like. The pulse is rapid and wiry, the leukocytes greatly increased and a febrile temperature present. The diagnosis of peritonitis is easily made, but the source presents greater difficulty. The tenderness may be most marked in the right iliac fossa, due to the gravitation of the fluid, and a diagnosis of appendicitis is made. A careful history and examination aid in differentiating, but usually an exploratory incision is necessary to determine the condition. Cases simulating perforation should have careful consideration before this possibility is excluded.

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# WAR MEDICINE

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## THE TACHYCARDIAS OF SOLDIERS.

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IN the present war it has been the experience of the European combatants that many men have broken down during the stress of active campaigning as a result of damaged or insufficient hearts which were unable to bear the additional strain thrown upon them by the campaign. Many of these heart cases were invalided home on account of frank cardiac disease, valvular disease unrecognized through insufficient examination at the time of the physical examination upon entering the army or myocardial disorders unsuspected or developing after entry into the army. There were, however, many returned to home hospitals

in whom actual organic cardiac disease could not be demonstrated, yet who suffered from a group of symptoms which were for the most part almost entirely referable to the cardiovascular apparatus and to which various terms have been applied, suggestive of the part played by the heart in producing and maintaining these symptoms. This symptom-complex is referred to by the English as "disordered action of the heart (D. A. H.)," as the "irritable heart of the soldier," as "soldier's heart" and as "effort syndrome." The terms are very inclusive, and practically any case with subjective cardiac symptoms, no matter what the cause, sufficiently severe to prevent the man carrying on his duties as a soldier, is listed as D. A. H., provided that the objective symptoms are not sufficiently marked to enable the physician to label the disorder as a definite nosological entity. As a result of this rather indiscriminate filing of indefinite cases into the one cabinet there is considerable confusion in the English and French literature as to just what is "soldier's heart." Certainly there is decided confusion as to the pathogenesis of the condition and as to what cases should be included etiologically. Most observers are, however, united in describing the same group of symptoms for the condition, but are divided, necessarily, owing to the obscurity of the etiology, upon the question of proper treatment and the management of these cases.

There is one outstanding and notable symptom not only in organic cardiac disease but also in disordered heart action cases, and that is rapidity of the pulse. It is almost a *sine qua non* for the diagnosis of these latter cases. Because of this and because of the ease with which it is appreciated in physical examination it is an extremely important symptom, but unfortunately one which may be interpreted in many ways. A rapid pulse is only a symptom, and it may be indicative of an infection, of disordered nervous mechanism or of a disturbance of the endocrine system as well as pointing to the heart itself.

On account of the large number of soldiers with tachycardia that were referred for opinion during the course of the cardiovascular examinations of the 38th Division at Camp Shelby, it was thought advisable to devise a working classification for these cases in order to attempt to classify them, with the idea that these sufferers with tachycardia could be grouped into one of several etiological classes and that the subsequent course in the army of these men could be followed from the stand-point of their ability to carry on their duties as a soldier. The latter part of this paper will deal with the classification that was used during the examination. In the first portion of the article will be discussed the English and French experiences with soldiers suffering with tachycardia, and more especially "disordered action of the heart" or "soldier's heart."

### SOLDIER'S HEART.

The recognition of this syndrome by no means is original to the present war, but was first described by Dr. Henry Hartshorne,<sup>1</sup> to be followed several years later by the classical paper of J. C. Da Costa,<sup>2</sup>

<sup>1</sup> On Heart Disease in the Army, Tr. Coll. Phys., Philadelphia, AM. JOUR. MED. SC., 1864, xlviii, 89.

<sup>2</sup> On Irritable Heart. A Clinical Study of a Form of Functional Cardiac Disorder and its Consequences, AM. JOUR. MED. SC., 1871, lxi, 17.

who describes the symptom-complex most accurately; in fact, his description tallies closely with the present-day picture of the disorder. In the succeeding years there has been more or less written about "soldier's heart," and none of it of much value. Although war broke out in 1914, the first reference to the condition is in an article by Magnus-Levy,<sup>3</sup> who notes the frequency with which the wounded complain of dyspnea, precordial pain and palpitation, and with which they show a tachycardia, poor response to exercise, increase in the area of cardiac dulness and systolic murmurs. This article was followed by many others in the German literature. In English literature the earliest reference to the condition is in an editorial of the *British Medical Journal*, July 17, 1915. In November, Thomas Cotton, Thomas Lewis and F. H. Thiele<sup>4</sup> published a short note on the occurrence of bacteria in the urine of sufferers with irritable heart. Succeeding this article has come forth a veritable stream of articles on the subject, culminating in the splendid, thorough, comprehensive and scholarly study of Thomas Lewis and his co-workers working under the auspices of the Medical Research Committee.<sup>5</sup> In this monograph all the various phases of the subject are considered in detail and a large amount of clinical and experimental work incorporated, so that one interested in the subject will find there an extremely complete discussion of the etiology, symptomatology, pathology, prognosis and treatment of soldier's heart.

It will be advisable to digest in brief this report and to incorporate the opinion of others upon these subjects.

**DEFINITION.** Major McEakins,<sup>6</sup> Lewis and their associates give the following definition of "irritable heart of soldiers:" "We use it (the term irritable heart) to describe those patients in whom few or none of the graver signs of heart affection can be detected but in whom there is complaint of breathlessness, palpitation, giddiness or actual fainting, easy exhaustion and precordial pain in varying degree, symptoms arising for the most part under exertion or exaggerated by it."

In later publications Lewis prefers to use the term "effort syndrome," believing that it is unwise to label this group of symptoms with a term which suggests to the soldier and to others that the heart is primarily at fault.

A somewhat more comprehensive definition of soldier's heart than the one recorded above might be given. A syndrome of symptoms referable for the most part to the heart, induced by too strenuous preliminary training or the mental and physical stress of actual warfare appearing in those soldiers who have suffered a recent infection and predisposed to by various factors of varying value, such as previous sedentary life, larval hyperthyroidism, undetectable myocardial disease or congenital myocardial insufficiency, unstable nervous system, subject to neuroses of different types, and excessive smoking (?)

<sup>3</sup> Berl. klin. Wehnsehr., January 11, 1915.

<sup>4</sup> A Note on the Irritable Heart of Soldiers, *British Med. Jour.*, November 13, 1915, p. 722.

<sup>5</sup> Report upon Soldiers Returned as Cases of Disordered Action of the Heart (D. A. H.) or Valvular Disease of the Heart (V. D. H.), 1917. London: Causton & Sons.

<sup>6</sup> A Memorandum upon Heart Affections in Soldiers, *British Med. Jour.*, September 23, 1916, p. 418.



**ETIOLOGY. Previous Occupation.** In Lewis's series of 543 cases 57 per cent. were engaged in sedentary occupations, 20 per cent. in moderately severe physical occupations and 23 per cent. in hard manual labor before entering the service. It is noteworthy that those used to hard physical work make the most satisfactory recovery.

**Infection.** Lewis lays particular stress upon infection as the most important etiological factor. In from 50 to 60 per cent. of his cases infection played an important role. It was during the convalescence from an acute infection that the symptoms first appeared in the greatest number of cases. Others had suffered previously from some acute infectious disease of marked severity, as pneumonia, rheumatism, typhoid fever. John Parkman<sup>7</sup> in a series of 40 cases found in 12 patients a previous history of an infection which may have been the exciting cause of the condition. Seven said they had had scarlet fever in childhood and 5 developed symptoms immediately following an illness in military service. Sir James Mackenzie<sup>8</sup> says that in the examination of about 400 cases of soldier's heart he has attributed the majority of these cases to bacterial and toxic influences. R. McN. Wilson<sup>9</sup> is in complete accord with Mackenzie, and L. Gallavardin<sup>10</sup> agrees that infections have a very decided influence upon the development and exaggeration of nervous tachycardias.

**Shock.** This was an immediate cause in only 2 per cent. of Lewis's cases, shock in all likelihood acting as a remote cause on a condition already existing.

**Wounds and Other Accidents.** These factors were present in 5 per cent. of Lewis's series. As in shock these accidents probably act much the same way. Added to this there is the added factor that most wounds are associated with infection.

**Poisoning by Gas.** This cause instituted the onset of symptoms in 3 per cent. of the Hampstead Hospital cases. Price and Hunt have called attention to the fact that certain gases may induce the syndrome either as a result of the action of the gas on the nervous system or else as a result of the febrile pulmonary complications of gas poisoning.

**Sudden Overstrain.** The occurrence of this factor was relatively rare, less than 1 per cent., in causing the onset of symptoms. A. Abrahams<sup>11</sup> is not in accordance with this view, he believing that this is responsible, in a fairly large number of cases, for the complex.

**SYMPTOMATOLOGY.** Mackenzie's<sup>12</sup> description of the onset of symptoms deserves to be quoted: "The account given of the onset of the symptoms is peculiarly instructive. They will say they were in the trenches and felt well and fit until one day they felt seedy and ill, and this continued until they were compelled to seek medical advice, when they were found to have a raised temperature. A few days' relief was obtained and they returned to their work still feeling far from well, and after a few weeks of the strenuous life in the trenches they collapsed, sometimes with loss of consciousness, breathlessness or even pain.

<sup>7</sup> The Cardiac Disabilities of Soldiers on Active Service, *Lancet*, London, July 22, 1916, p. 133.

<sup>8</sup> The Soldier's Heart, *British Med. Jour.*, January 22, 1916, p. 117.

<sup>9</sup> The Irritable Heart of Soldiers, *British Med. Jour.*, January 22, 1916, p. 119.

<sup>10</sup> Les tachycardiques, *Arch. de mal de coeur*, September, 1917, p. 408.

<sup>11</sup> Soldier's Heart, *Lancet*, London, March 24, 1917, p. 412.

<sup>12</sup> *Loc. cit.*

"The story of the onset varies. Sometimes it is an attack of diarrhea, which persists for a time; sometimes it is after a definite illness, as measles, but most give a history which we can safely surmise as being due to an infection. In a few cases one cannot get such a definite account of the starting of the illness, but many do recognize the gradual onset of the trouble. That is the story of the majority of cases, but there are a number from whom we can get no suspicious history of infection but in which there is an account of a very strenuous life."

*Symptoms in Detail.* Practically all observers are united in describing the same subjective and objective manifestations of the disorder, but the Research Committee's report by Lewis is so complete that it will suffice to secure a complete picture of the condition to abstract it and use it as the basis for the description of the symptomatology.

*Dyspnea.* This is complained of by all patients after effort; when quiet the patient does not notice it except in an occasional case of nervous, rapid breathing, but slight effort brings this out so that the respirations are increased moderately, while more severe effort will cause a rise of respiratory rate to 60 to 70 per minute.

Lewis,<sup>13</sup> in discussing the cause of breathlessness in patients suffering from irritable heart, expresses the opinion that it is due to the inadequate supply of buffer salts in the blood. He shows that he and his co-workers have demonstrated this, and calls attention to the fact that this symptom of breathlessness arises as a result of disordered metabolism, though the commonly accepted cause of breathlessness has been held to be instability or irritability of the central nervous system. This inadequate supply of buffer salts permits overstimulation of the respiratory center by the CO<sub>2</sub> developing as a result of exercise. There is an insufficiency of these salts, consequently their buffer effect is lost and the CO<sub>2</sub> is able to act more directly upon the center than if these salts were present to neutralize and to overcome the direct shock of the acid CO<sub>2</sub> upon the center.

*Pain.* This is another very constant symptom, occurring in over three-quarters of all cases. The pain is of different degrees, varying from slight precordial distress to severe pain over the entire preeordium and transmitted down the left arm. The pain is induced by exercise. J. C. Meakins and E. B. Gunson<sup>14</sup> have shown that in 48 per cent. of soldiers with irritable hearts, complaining of severe pain, there is nearly always present an area of hyperalgesia over the left chest in front. This hyperalgesia is similar to that seen in cases of angina pectoris; it is increased by exertion; infection increases the precordial pain and hyperalgesia; and the presence of precordial hyperalgesia is indicative of severe cases, with poor prognosis.

*Palpitation.* This is also a very common symptom. In the great majority of cases it is due solely to the increased rate of the heart after exercise and disappears as soon as the heart rate slows down. Occasionally palpitation is due to extrasystoles which appear during rest to disappear during exercise.

<sup>13</sup> Breathlessness in Soldiers Suffering from Irritable Heart, British Med. Jour., October 14, 1916, p. 517.

<sup>14</sup> The Occurrence of Hyperalgesia in the Irritable Heart of Soldiers, Heart 1917, vi, 343.

*Cerebral Symptoms.* Vertigo occurred in about 75 per cent. of the patients. The patients were dizzy after exertion, the dizziness being accompanied by spots of light in the visual field. It was always pronounced when changing from prone to upright position quickly. This probably induced a sudden fall in intracranial pressure, though it is not always possible to show a fall; indeed, a rise in peripheral systolic pressure is seen at times.

*Syncopal attacks* were found to occur in six subjects. The pulse rate was slowed, though attacks did not altogether resemble those found in Adams-Stokes's disease, and the systolic blood-pressure was likewise much lowered.

*Sweating and Salivation.* The subjects of soldier's heart were found at rest to have moist sweating hands, and during the physical examination, sweat would run down from the axillary sweat glands. Physically effort would induce sweating out of all proportion to the degree of exercise as would a stimulation of the emotions. An increased amount of saliva was also thought to be secreted. T. F. Cotton, J. G. Slade and Thomas Lewis<sup>15</sup> conclude, from a series of studies upon these men after injections of pilocarpin nitrate, that "the increased activity of the sweat glands and the increased activity of the salivary glands (as estimated by the rate of swallowing) of patients suffering from "irritable heart" appear to be due to hyperexcitability of the corresponding peripheral mechanisms."

*Vasomotor Symptoms.* Spontaneous flushing is induced by the slightest cause. Cotton, Slade and Lewis<sup>16</sup> say, as a result of their studies with amyl nitrite, that this spontaneous flushing is "conditioned more often by the state of the peripheral vessels than by hyperirritability of the nervous system."

*Pulse Rate.* The increase of the pulse rate upon effort is one of the most characteristic symptoms found by Lewis and his co-workers. Furthermore, it is an extremely valuable objective finding in cases which may have complaints suggestive of the disorder but in whom these complaints might be due to other causes. Slow recovery of the pulse rate to what it was before exercise is a bad prognostic sign, though quick recovery is not necessarily a sign that ultimate fitness will be attained by proper treatment. J. C. Meakins and E. B. Gunson<sup>17</sup> show that before the simple test exercise (walk 75 paces at quick time ending in a climb of 27 steps) the average pulse rate was 86 per minute (controls 75), the rise after exercise 131 (control 110), the length of time of the return of the pulse rate to normal was in direct ratio to the severity of the symptoms. They also found that rest in bed and intercurrent acute infections have a most deleterious effect upon the return of the pulse rate to normal after exercise. John Parkman<sup>18</sup> found that after slight exertion and on standing the average increase in pulse rate was greater in these patients than in the controls.

<sup>15</sup> Observations upon Pilocarpin Nitrate, *Heart*, 1915-17, vi, 299.

<sup>16</sup> Observations upon Amyl Nitrite, *Heart*, 1915-17, vi, 311.

<sup>17</sup> The Pulse Rate after a Simple Test Exercise in Cases of Irritable Heart, *Heart*, 1915-17, vi, 285.

<sup>18</sup> The Pulse Rate on Standing and on Slight Exertion in Healthy Men and in Cases of Soldier's Heart, *Heart*, 1915-17, vi, 319.

*Blood-pressure.* The blood-pressure at rest is usually about normal. The effect of a fixed amount of exercise upon blood-pressure shows that the reaction is qualitatively the same, but the pressure rises higher and the raised pressure is longer sustained in the patients than in controls.<sup>19</sup>

*Effect of Drugs.* Digitalis, according to J. Parkman,<sup>20</sup> has scarcely any influence in this condition and is not indicated. Adrenalin, a sympathetic stimulator, was found to have a greater effect upon the heart sympathetic than in the normal, while apocodein, a sympathetic depressor, caused similarly a greater depression.

*The Physical Examination.* Aside from the pulse rate, physical examination seems to disclose but little in these cases. In fact, the absence of physical signs is one of the negative symptoms of value. In the Hampstead Hospital Report, Lewis goes into the question of systolic murmurs with considerable thoroughness. He shows that systolic murmurs *per se* have but little importance. Two hundred and sixty-six soldiers did not show any murmurs, and of these 58 per cent. were definitely unable to be restored to duty, while of 196 soldiers with systolic murmurs only 51 per cent. were unfit for duty. Meakins, Lewis and others<sup>21</sup> say that "A systolic murmur at the apex is not considered to be a sufficient ground for discharge, whatever the character of the murmur; in our experience many men who present this sign are capable of a great deal, if not of full and continued effort."

In these sentiments the authors are in accord with Sir James Mackenzie, who holds that the functional capacity of the heart is the criterion upon which hearts must be judged, not the presence or absence of murmurs. This view-point of Mackenzie, long held by him, but brought to the fore by his advice to medical examiners not to reject men with heart murmurs unless their hearts showed definite signs of insufficiency or gross myocardial change, precipitated an active and at times even acrimonious debate among English cardiologists and clinicians. The work of Lewis would seem to support Mackenzie's contention most completely, though the controversy still is active in English periodicals.

*The Apex Beat.* Extension of the apex beat downward only shows that there is hypertrophy of the heart and does not help in determining the functional capacity of the organ. Likewise the force of the beat, its definite localization or diffuseness has no value in making the above determination.

*The Size of the Heart.* The report of the Medical Research Committee contains some interesting roentgenological observations by Meakins and Gunson upon the change in the size of the heart after exercise. In the normal individual active exercise results in a diminution in the diameter of the heart of about 1 cm. In patients whom the exercise caused the usual symptoms a decrease in the diameter of the heart was not noted, nor was there, however, any increase in size of the transverse diameter or dilatation, though the absence of the usual and normal diminution in size might be construed as a dilatation.

<sup>19</sup> T. Cotton, D. L. Rapport and Thomas Lewis: After-effects of Exercise on Pulse Rate and Systolic Blood-pressure in Cases of Irritable Heart, Heart, 1915-17, vi, 269.

<sup>20</sup> Digitalis in Soldiers, with Cardiac Symptoms and a Frequent Pulse, Heart, 1915-17, vi, 321.

<sup>21</sup> Loc. cit.

*Electrocardiographic Studies.* These showed no variations other than occur in certain normal individuals. The tracings are of no value in diagnosis nor in prognosis.

*Leukocytosis.* One of the most valuable objective signs of the presence of soldier's heart is found in the leukocyte count. G. Briscoe<sup>22</sup> found that in cases of irritable heart there was a constant leukocytosis when the patient was up and about and increased by exercise. She found that this was slight or there was none at all during absolute rest. The degree of leukocytosis seemed to be in direct relation to the severity of the case. Thus in the 4 most severe cases clinically the counts after exercise varied between 18,000 to 23,000 as contrasted with the 4 least severe cases which showed after exercise a moderate increase, 8700 to 13,700. The rise after exercise is in all cases greater than in normal controls.

In regard to the differential count she noted a higher lymphocytic count in cases of long standing, though the highest values were obtained in a case of only six weeks' duration. The percentage rise in lymphocytes may be marked in patients who show only a slight leukocytic increase after exercise. Furthermore, the variability of the several kinds of leukocytes is greater than in normal individuals. The author also calls attention to the fact that while the leukocytosis is of value in diagnosis, being uncontrolled by the patient, in prognosis it is of not much assistance, as the condition of the blood varies with the general condition of the patient, which can be judged by the usual clinical methods.

*Urine.* The total quantity is usually reduced. In 60 per cent. of the cases the acidity was greatly increased. In general, amino-acids, calcium and oxalic acid are increased; phosphates and urea decreased; uric acid, creatinin, sulphates normal.

It has been suggested that the amino-acid increase might be correlated with the urea decrease as an indication of functional liver trouble.

The urinary acidity in normal controls is unchanged after exercise to increase slightly one to one and a half hours afterward, while in these subjects of soldier's heart the acidity falls after exercise to increase very much more than the normal controls in an hour to an hour and a half.

*Prognosis.* While the present article is concerned chiefly with the symptoms and the causative factors of this condition it might be well to briefly consider Lewis's figures as to ultimate serviceability of these men: 63 per cent. of the men coming from training camps are definitely unsuitable to carry on their full duties as soldiers and but 48 per cent. when they come from active service; 64 per cent. of those who had symptoms before enlisting are unsuitable for future service; 48 per cent. are unsuitable whose first symptoms appeared at time of training and 40 per cent. whose symptoms appeared during active service. Among those who performed manual labor before entering the service, 48 per cent. and those who led a previous sedentary life 53 per cent. were unsuitable to be returned to duty. Lewis also says that the symptoms existed in 43 per cent. before enlistment, 12 per cent. developed them during the training period and 45 per cent. during active service.

*TREATMENT.* Detailed treatment will not be considered. Suffice it is to say that rest in bed is distinctly contra-indicated. Gradually

<sup>22</sup> The Leukocytes in Cases of Irritable Heart, *Lancet*, London, June 2, 1917, p. S32.

increasing exercise has given the best results to all observers, though A. E. Garrod<sup>23</sup> has called attention to a group of cases in which the myocardium is involved as a result of some fresh or recent infection and in whom exercise is contra-indicated and rest in bed indicated.

**PATHOGENESIS.** The pathogenesis of soldier's heart has aroused so much discussion in England, as already mentioned in the forepart of this paper, that it may be well to discuss the various hypotheses advanced to explain the condition.

**I. Blood Infection.** As recounted earlier in this paper Cotton, Lewis and Dale<sup>24</sup> aroused interest in the possible infectious origin of soldier's heart by describing the occurrence of an almost constant bacilluria in these cases and at times bacillemia. Subsequent work failed to confirm this, and G. Briscoe and L. Demoud<sup>25</sup> put at rest this theory by making 96 observations on 43 cases of irritable heart at the Hampstead Military Hospital, none of the cultures proving positive when a careful technique was evolved.

**II. Overstrain of Heart.** That sudden severe or continuous overstrain of the heart may occasion soldier's heart is a possibility in rare cases, but in the majority of cases surely there is no such possibility. Sir Clifford Allbutt<sup>26</sup> says that "heart strain," a phrase at one time, a few years ago, in common use, is a rare event and does not constitute the bulk of the cases invalided home as D. A. H. Thomas Lewis<sup>27</sup> says that the condition originated in sudden effort in only 5 cases that he had seen. Effort aggravates the symptoms and displays defects which are latent, but that it is responsible for the condition is not to be believed from present evidence. The strongest evidence of damage by strain must be forthcoming before it can be believed that so vital a muscle as the healthy heart can be injured by strain. Sir James Mackenzie says that "I never saw a single individual who suffered from heart dilatation as a result of overexertion. I think I may fairly say that this was not due to inability to recognize overstrain." In this article, in which Captain A. Abrahams<sup>28</sup> quotes Mackenzie, he (Abrahams) says that he has never seen a case of overstrain in the examination of many athletes' hearts. Captain J. Parkinson<sup>29</sup> says that among his 40 cases only 4 attributed the onset of symptoms to a particular exertion, and 3 of these cases had had recent influenza. Contrary opinions as to the likelihood of strain causing symptoms of cardiac insufficiency are held by others. Captain W. Scarisbrick<sup>30</sup> in his paper on the comparative incidence of heart disease among soldiers and recruits finds 26.6 per cent. of the former and 15.2 per cent. of the latter suffering with "strained hearts." Dr. I. Mackenzie,<sup>31</sup> however,

<sup>23</sup> A Variety of War Heart which Calls for Treatment by Complete Rest, *Lancet*, London, June 30, 1917, p. 985.

<sup>24</sup> *Loc. cit.*

<sup>25</sup> Bacteriological Examination of the Blood in Cases of Irritable Heart, *British Med. Jour.*, August 18, 1917, p. 210.

<sup>26</sup> The Investigation of the Significance of Disorders and Diseases of the Heart in Soldiers, *British Med. Jour.*, August 4, 1917, p. 139.

<sup>27</sup> Soldier's Heart, *Lancet*, London, March 31, 1917, p. 510.

<sup>28</sup> *Ibid.*, March 24, 1917, p. 442.

<sup>29</sup> Cardiac Disease in Soldiers and Recruits, *British Med. Jour.*, February 24, 1917, p. 254.

<sup>31</sup> The Soldier's Heart, *Glasgow Med. Jour.*, 1916, lxxxvi, 213.

<sup>29</sup> *Loc. cit.*

believes that there is no evidence to show that in cases of soldier's heart the disease has resulted from strain of a physical character. In work done before the war, Moritz, de la Camp, Selig and many other German observers claim that the heart cannot dilate under the influence of muscular tension.

III. *Hyperthyroidism*. The hypothesis that the overaction of the heart is due to oversecretion of the thyroid gland is one that appeals to many observers of the condition, nor is this view-point a surprising one when the marked similarity of the symptoms of early Graves's disease to those of the irritable heart of the soldier is considered. One of the foremost advocates of this theory in part is Dr. J. Strickland Goodall,<sup>32</sup> who states in his Chadwick Lecture, based on 2250 cases of soldier's heart, that many cases of soldier's heart are due to the temporary overaction of the suprarenal glands as a result of fright, with a resulting overaction of the thyroid to neutralize this stimulation of the suprarenals. The thyroid overaction persists, the suprarenals overaction is but temporary. Captain Searisbrick<sup>33</sup> says that in some of his cases hyperthyroidism accounted for the cardiac neuroses. H. J. Leeuwen,<sup>34</sup> working under Major Tait McKenzie, found the thyroid enlarged in about 25 per cent. of his cases, and states that some of his cases suffered from hyperthyroidism. Wilson,<sup>35</sup> Sir James Mackenzie's assistant, says that while the theorists are bankrupt the disease remains. In 18 of his cases, however, he was interested in observing that the thyroid was enlarged and administration of thyroid caused exacerbation of the symptoms. Sir James Barr<sup>36</sup> says that it is no wonder that, under present conditions of war, we should get great vascular disturbance and increased function of the thyroid gland. He says that all these cases of soldier's heart depend upon an increase or decrease of the internal secretion of the thyroid and that the proper treatment in these cases is that used in the treatment of hyperthyroidism or hypothyroidism. This paper of Barr's provoked considerable discussion in the literature, pro and con, as to whether the thyroid was necessarily at fault in all cases. Dr. F. A. Stoney,<sup>37</sup> working at the Fulham Military Hospital, believes that there is a very close relation between hyperactivity of the thyroid gland and the tachycardia and breathlessness seen in cases of irritable heart. In addition to the rapid pulse and breathlessness, together with the sinus arrhythmia and apical systolic murmurs, there is also noted tremor, insomnia, enlargement of one or both lobes of the thyroid and, more rarely, ocular symptoms. She believes likewise that a cure may be effected by securing partial atrophy of the thyroid gland with the roentgen rays. C. P. White and F. Hernaman-Johnson<sup>38</sup> also contend that hyperthyroidism is the cause of soldier's heart and treatment by the roentgen rays should not be neglected.

<sup>32</sup> The Factors of Cardiac Irritability, *Lancet*, London, June 23, 1917, p. 962.

<sup>33</sup> *Loc. cit.*

<sup>34</sup> The Heart and Active Service, *Lancet*, London, September 2, 1916, p. 432.

<sup>35</sup> Irritable Heart of Soldiers, *British Med. Jour.*, January 27, 1916, p. 119.

<sup>36</sup> The Soldier's Heart and its Relation to Thyroidism, *British Med. Jour.*, April 15, 1916, p. 544.

<sup>37</sup> On the Connection between Soldier's Heart and Hyperthyroidism, *Lancet*, London, April 8, 1916, p. 777.

<sup>38</sup> Hyperthyroidism as a Cause of the Irritable Heart of the Soldier, *Lancet*, London, January 8, 1916, p. 78.

Among the French, Gallavardin<sup>39</sup> also believes that in some cases the thyroid may be at fault, though this explains only some of the cases. D. Pletnew,<sup>40</sup> on the contrary, says that he has almost never seen it. Lewis<sup>41</sup> summarizes the opinions against incriminating the thyroid as follows: In spite of the frequency with which the thyroid is said to be enlarged by advocates of the hyperthyroid hypothesis, in his series of cases only 4 per cent. showed this sign; the symptoms of tachycardia, tremor and so on are seen after infectious diseases, and the thyroid is not asked to explain them; roentgenotherapy gives too doubtful results to be good evidence; and finally thyroid extract given experimentally seems to have no more effect on these cases than on other unrelated cases.

IV. *Disturbance of Nervous System.* All authors agree that the nervous element plays a more or less important part as an excitant of the disorder. Mental stress is if not a greater at least an equal factor with physical stress in exciting the attack. Some writers claim it is the entire and sole cause. For example, Dr. I. Maekenzie<sup>42</sup> says that the soldier's heart in all probability belongs to the disorders of psychic origin. Tullidge<sup>43</sup> also calls attention to the psychic origin of the neuroses. R. D. Rudolf<sup>44</sup> says that "the condition is in reality part of a general nervous instability—in other words, neurasthenia." Dr. Poynton<sup>45</sup> believes that nerve shock is a factor of importance in some cases. Alexander Morrison,<sup>46</sup> in discussing the question as to the pathogenesis of the condition, says that in his belief the condition is one of neurasthenia or psychasthenia. Sir William Ewart<sup>47</sup> holds that the heart may collapse as a result of gradual exhaustion of the myocardium, myocardial failure or as a result of some overwhelming shock in a nerve-worn subject, functional heart stroke, and that "soldier's heart" is probably a combination of these two factors.

Lewis discusses the hypothesis of the nervous system causing the condition in brief as follows: In general the subjects of cardiac irritability are emotional, high-strung individuals with exaggerated reflexes. Vagal tone is not abolished, as experiments with atropin show, but that the vagus action is normal is questionable because the pulse fails to return to normal after exercise, because sinus (vagal) arrhythmia is often exaggerated in many cases and because syncopal attacks with extreme slowness of heart occur in some cases. On the other hand, lack of vagal tone does not appear to be responsible in irritable hearts, for the high pulse rate or the exaggerated response to exercise, rather a hyperirritability of some portion of the system which includes the acceleration reflex arc and the rhythm-producing center itself. Experiments with adrenalin and apocodein show that the sympathetic system is more easily stimulated or depressed than normal in those individuals

<sup>39</sup> Loc. cit.

<sup>40</sup> Insuffisance cardiovasculaire . . . de la guerre, Arch. de mal de coeur, 1916, ix, 333.

<sup>41</sup> Loc. cit.

<sup>42</sup> Loc. cit.

<sup>43</sup> The Heart of the Recruit and the Soldier, Military Surgeon, 1917, xl, 24.

<sup>44</sup> The Irritable Heart of Soldiers, Canadian Med. Jour., 1916, vi, 796.

<sup>45</sup> British Med. Jour., January 22, 1916, p. 130.

<sup>46</sup> Ibid., 1911, p. 184.

<sup>47</sup> The Soldier's Heart and the Strained Heart, British Med. Jour., February 5, 1916, p. 218.



suffering with irritable hearts. In all probability these variations in nervous excitability are secondary to changes in cellular metabolism or to true intoxications.

V. *Myocardial Lesions.* At the Hampstead Hospital it is the custom to sift out all cases of frank valvular and of myocardial diseases, referred there as D. A. H., before listing the remaining cases as having irritable hearts. In spite of this many of the cases of the irritable heart of soldiers gave a history of previous rheumatism or chorea, suggesting that mild myocardial lesions may give rise to the symptoms. Autopsy alone would be able to verify this. The electrocardiogram was unable to show any such evidence of myocardial disease in 10 cases examined by Parkinson. It does seem, however, hard to conceive of acute rheumatic fever leaving the heart muscle untouched, and it would seem that in these cases at least the myocardium was involved. Parkinson<sup>48</sup> in his study of 40 cases of soldier's heart excluded frankly diseased hearts. He believes that the relative cardiac insufficiency may be a sequel to certain acute infections, may be the result of myocardial changes due to age, may be associated with functional nervous disorders and may be due to endowment with a heart of limited efficiency. Garrod<sup>49</sup> calls attention to the fact, also, that there are certain cases of soldier's heart, following immediately after acute infections, in whom "the myocardium is damaged for a time." He concludes his article by saying that "the soldier's heart is not a clinical entity but includes a variety of morbid states."

Another phase of the question of the heart itself may be here considered, that is, the heart that is distorted in position or hypoplastic. Goodall<sup>50</sup> says that hearts showing persistent overexcitability of muscle or nerve are too horizontal in position because they are too soft. This lack of tone may be the result of impaired nervous control, habitual overwork with insufficient rest, or disuse, insufficient use or misuse. D. Pletnew,<sup>51</sup> in concluding his article on cardiovascular insufficiency in the war, says that the greatest number of soldiers who present the phenomena of cardiovascular insufficiency are individuals in whom early arteriosclerosis is appearing or whose heart and aorta are hypoplastic. In addition to insufficient development of these organs the disharmonious development of the different organs, plays an important part in the pathogenesis of insufficient heart. This latter develops most frequently among well-built men who have not been accustomed to muscular exercise. It might be added here that many of the English authors also call attention to the necessity of starting military training with mild exercise gradually increased.

VI. *Toxemia.* The hypothesis that a toxemia is the agent responsible for the disorder is the one accepted by Lewis as seemingly the most feasible. Receiving as it does the approval of Mackenzie<sup>52</sup> and Allbutt, as well as Lewis and his co-workers, who have studied the question so carefully from all angles, it is needless to state the hypothesis that is most generally accepted both in England and France.

<sup>48</sup> Loc. cit.

<sup>49</sup> A Variety of War Heart, *Lancet*, London, June 30, 1917, p. 984.

<sup>50</sup> Loc. cit.

<sup>51</sup> Loc. cit.

<sup>52</sup> The Soldier's Heart, *British Med. Jour.*, January 22, 1916, p. 117.

This hypothesis is based on the following facts: Most of the cases started from some infection; the symptoms are analogous to those appearing in convalescence from acute infections or in the early stages of pulmonary tuberculosis; the changes of the urine and of the blood, mentioned in the forepart of this paper, suggest an infection. This hypothesis assumes either the production of true toxic bodies acting on the heart or disorders of cellular metabolism resulting from the infectious process.

In closing this discussion of irritable heart it might be appropriate to insert here, while considering the toxic hypothesis, some remarks Sir Clifford Allbutt<sup>53</sup> made upon the researches of Dr. Lewis and his associates at Hampstead Hospital: "Setting aside for the while poisoning of the myocardium, may incidental infections produce any other effects in which the heart is concerned? The answer appears to be in the affirmative. These researches seem to discover a new disease, or rather to discriminate more exactly the features and nature of a disease less clearly apprehended already, by Da Costa and others as soldier's heart; or by those of us who have written upon neurasthenia as cardiac neurasthenia. The disease is one which is not uncommon in the civil population, but under the stress of the soldiers' training and among the aggregations of men in modern armies, it is more conspicuous and inconvenient."

**CLASSIFICATION OF TACHYCARDIAS USED IN EXAMINATION OF THE SOLDIERS OF THE THIRTY-EIGHTH DIVISION.** Before discussing the classification of the large number of cases of tachycardia seen during the course of the cardiovascular examination at Camp Shelby, it may be well to sketch briefly the method of procedure in making the cardiovascular examinations. The cardiovascular examiner worked in conjunction with the tuberculosis board which examined practically every man in the command. The several members of this board in examining the thorax would percuss and auscult the heart at the same time they were going over the lungs. Any abnormality that they might detect in the heart, such as abnormalities in the cardiac impulse, excessive rapidity or slowness, murmurs, irregularity, accentuations and enlargements, was sufficient to refer the individual with the abnormal condition to the cardiovascular examiner. When a man was referred for cardiovascular examination a note was sent with him stating for what reasons he was referred. The examiner working alone in a separate room of the regimental infirmary then went over the soldier carefully and studied the condition thoroughly in order to determine the effect that it might have upon the soldier under the stress of active campaigning.

In addition to the usual methods of physical examination the functional strength of the heart was estimated by having the examinee hop seventy times on one foot. The pulse was counted before the hopping test, immediately afterward and two minutes later. A return of the heart rate preceding exercise, provided that immediately following exercise there was an increase in rate, was considered evidence of good functional capacity of the organ. In reference to this exercise test of functional sufficiency of the heart, which is recommended by the

<sup>53</sup> Loc. cit.

Surgeon-General's Office and which is generally considered the best test of cardiac sufficiency, it might be well to quote Meakins, Lewis and others.<sup>54</sup> "It has been our special endeavor to find some relatively simple and quick test which will eliminate the unfit, and for this purpose we have made elaborate observations upon pulse rate, blood-pressure and respiratory rate under various conditions of posture and exercise. We have taken numerous instrumental records, polygraphic and electrocardiographic; we have also noted such physical signs as basal murmurs, jerky impulse, extended impulse, various alterations of the heart sounds and signs of vasomotor instability; with a solitary exception we find these to be of no value in gauging the grade of exercise which will be ultimately tolerated or readily be borne. The solitary exception is the rate at which the pulse falls when it is accelerated by a brief exercise." C. Lian,<sup>55</sup> in France, is also an advocate of this method of testing the functional efficiency of the heart while in this country. T. B. Barringer, Jr.,<sup>56</sup> has done a great deal of work upon this same principle.

Nine hundred and forty-four soldiers, from the division of a strength of 22,622 at the time of the examination, were sent for special study of the cardiac condition. Of those thus referred, 424 (44.9 per cent.) were sent with the diagnosis of "tachycardia." It is thus seen that a very large number of the cases studied were cases of a rapid heart action. In fact, the provisional diagnosis of tachycardia exceeded by a large number any other single diagnosis. The heart rate was determined by counting the number of systoles heard by the stethoscope over the precordium in thirty seconds. The cardiovascular examiner was authorized by the Surgeon-General to act upon these cases in three ways, either unconditionally to "reject" or to "accept" the examinee as a soldier, or to "accept conditionally," with the idea that a future examination would show if the condition had so improved under training that the man could carry on the duties of a soldier.

In the study of the 424 cases of tachycardia seen at Camp Shelly it was obvious that an opportunity was afforded of classifying these possible future cases of soldier's heart before the actual onset of the trouble. In other words, an etiological factor might be determined ante rather than post, as was necessary in the English studies. Furthermore, by classifying these subjects with rapid heart it would be possible more satisfactorily to dispose of them in one of the three ways recommended by the Surgeon-General's Office, namely, accept, reject or accept conditionally. One may rightly judge, from the various hypotheses concerning the pathogenesis of soldier's heart discussed in the forepart of this paper, that there is still considerable haze as to the true factor in the production of the disorder. In spite of Lewis's masterly work there still seems, for example, a strong possibility that the thyroid may be implicated in a certain number of cases. Likewise it seems quite definitely proved that soldier's heart, while excited by an infection,

<sup>54</sup> *Loc. cit.*

<sup>55</sup> *Épreuve d'aptitude cardiaque à l'effort*, Presse méd., December 7, 1916, p. 563.

<sup>56</sup> *The Circulatory Reaction to Graduated Work as a Test of the Heart's Functional Capacity*, Arch. Int. Med., 1916, xvii, 363. Also, *Studies of the Heart's Functional Capacity*, Arch. Int. Med., 1917, xx, 829.

is predisposed to by certain factors. The work of the English has all been done upon cases already the subject of soldier's irritable heart. There the predisposing or etiological factor had to be determined after the onset of the trouble, whereas in the present study it could be determined possibly before the trouble appeared, but as the question of the pathogenesis is still somewhat in doubt it was thought wise to classify these cases of tachycardia not from one view-point alone but to make a classification which would combine the best of the ideas as to the cause of "soldier's heart." Many of the cases of tachycardia that were seen during the course of the examinations seemed unlikely to develop "soldier's heart" and could be grouped in other classes.

The following five etiological classifications of the tachycardias were made: (1) Myocardial. (2) Hyperthyroid. (3) Neurotic. (4) Nervous (emotional). (5) Toxic.

These groups will be completely discussed seriatim, giving the number of cases in each group, their findings at the time of the examinations, the reason for classifying them in such a manner and their dispositions.

The first three groups represent cases that may develop "soldier's heart," the last two represent tachycardia of mild degree in whom it is believed no such result will obtain. These last groups will be discussed in the light of the experience of others more fully than the first three groups, which have been dwelt upon from this view-point in the early part of the paper.

1. *Myocardial*. Sixty-nine cases, or 16.3 per cent., of the tachycardias were of this type. The diagnosis was based upon the history of the individual, the physical findings and the functional tests. In considering the history, and it is in the individual with this type of rapid heart that the history is most important, it was noted that a large majority of these soldiers had suffered from pneumonia some time during the preceding five years, an interesting commentary upon the deleterious effect of pneumonia upon the heart. The present history was also important. The soldier suffered from dyspnea upon slight exertion, a cough was sometimes present and there were other subjective evidences of a very moderate degree of cardiac insufficiency. The physical examination, outside of the tachycardia, usually showed but little. At times a slight enlargement of percussion dulness was noted.<sup>57</sup> The functional test, the response to exercise was also of great value in determining this type of tachycardia. Failure of the pulse to return to normal within two minutes was considered an evidence of myocardial weakness and was the *sine qua non* in diagnosing these cases.

The disposition of the soldier with a rapid heart, presumably the result of myocardial change of a moderate degree such as outlined above, was usually "accept," as it was felt that the gradually increasing exercises of the training period would materially benefit the heart so

<sup>57</sup> It should be understood that frank cases of myocardial disease and cases of valvular heart disease with associated myocardial weakness were not listed in this group. These cases were diagnosed "myocarditis, chronic" and "valvular heart disease," and as such were considered. The above classification includes only those cases that are questionable. The term myocardial tachycardia is used because of the apparent slight degree of myocardial involvement. There was a history of pneumonia and there was a myocardial insufficiency, but that there was a true pathological myocarditis which could be demonstrable at autopsy could not be proved.

that he would be able to go through hardships of any type. Cases giving a history of acute rheumatic fever were rejected, as it is almost impossible to imagine the myocardium not being injured after this disease. Furthermore, Lewis found a large percentage (about 20 per cent.) of his cases of soldier's heart gave a past history of this disease.

2. *Hyperthyroid*. Ninety-seven cases of tachycardia attributable to malfunctioning of the thyroid, or larval hyperthyroidism, were seen. Three symptoms of hyperthyroidism were considered necessary to place a man in this group. Two of these symptoms were practically constant, a pulse rate of over 130 and a fine tremor; the third symptom was either enlargement of the thyroid or well-marked vasomotor symptoms. Exophthalmos was seen only a few times. The response to the functional test was usually poor. These cases were usually fairly easy to determine. Their disposition was, excepting in the well-marked unquestionable cases, which were rejected, generally "provisionally accept," as it seemed likely that these men would probably break down under the stress of trench warfare, developing exophthalmic goitre if not soldier's heart. If upon subsequent examination the symptoms have not disappeared it would seem wise to discharge them upon a surgeon's certificate of disability. An interesting point in regard to these cases was that a large percentage of them were found in a regiment recruited in the mountains of West Virginia. In this same regiment there were also found many men with symptomless goitres.

3. *Neurotic*. In this group fell the largest number of cases, 180 (or 42.5 per cent.). These men practically all presented the following syndrome: A pulse rate of over 120; an exaggerated sinus arrhythmia, and a functional heart murmur, systolic in tone, soft and blowing, heard best over the second and third interspaces, referred upward and to the subclavian artery, and never to the axilla. In discussing the murmur systolic in time, heard over the pulmonary valve area, H. M. Raven<sup>58</sup> says that in his experience with a camp of over 2000 boys under nineteen, a large number of them have this murmur. It is associated with poor physique and retarded development. He suggests that in addition to the commonly accepted theory that it arises as a result of friction between the pulmonary artery and the chest wall or adjacent structures, another theory might be advanced, that it is due to a relative or actual narrowing of the pulmonary artery (congenital). In these cases D. A. H. symptoms are very common.

The term neurotic is poor but was employed because these men all had many and diverse complaints of all kinds. Their subjective symptoms were pronounced, not only symptoms referable to the heart but symptoms which were indefinite, vague and uncertain, and referable to all parts of the body. Vagal might perhaps be a more satisfactory term, as they showed usually pronounced evidences of vagus instability. The majority of these men were listed as "conditionally accept." The experience of the English has shown that men falling into this classification are unable to stand the wear and tear and stress of severe campaigning. It is from this group that will probably come the most men who will develop the irritable hearts of soldiers. Their symptoms, their vagal instability, their heart examination, their rapid pulse rate,

<sup>58</sup> British Med. Jour., August 25, 1917, p. 251.

their poor response to the functional exercise test, all these findings are characteristic of the typical case of "soldier's heart." Indeed, they might readily be said to belong to that large class mentioned by Lewis in whom symptoms appeared before enlistment and who are not truly subjects of "soldier's heart," in the sense that the soldier's life is necessary to cause "soldier's heart." Some mild infection incurred before ever seeing active warfare may so exaggerate the symptoms that the man is no longer fit for active soldiering. It would be interesting to see how well these men respond to the splendid hygiene of camp life. Probably a goodly number will be so immeasurably benefited by the exercise, outdoor life, proper food, regular hours and careful life of camp that they will be able to go through with any future assignments they might receive. In the meantime by listing them as "conditionally accept" they will be under constant observation, and should they not be materially benefited by their new environment, should be kept in this country to perform military duties less arduous than those they will meet with overseas.

4. *Nervous (Emotional)*. The soldiers with rapid hearts who fell into this classification presented few objective or subjective manifestations of disordered heart. The tachycardia was not excessive, rarely over 120, physical findings were negative and the response to the functional test was normal. There were only twenty-eight men referred who were listed in this group. This may seem like a surprisingly small number, but it is small because such a diagnosis was made only when the pulse rate was unduly rapid. The men with the slower pulses were listed as "heart normal." The men of this group if allowed to sit quietly for twenty or thirty minutes to watch the examinations going on, in order to do away with the nervous excitement incident to the examination, and then examine them, their hearts would be found to have normal rates.

Two opinions as to the relatively innocuousness of this type of tachycardia may be mentioned. Sir James MacKenzie<sup>59</sup> calls attention in his brief memorandum to medical examiners to the effects of excitement. He states that many candidates with perfectly healthy hearts suffer from excited action of the heart during examination. The heart becomes rapid but soon slows down if the candidate lies down and breathes slowly and deeply for a few minutes. Such a candidate is considered suitable for enlistment if there is a history of good functional efficiency. A. Morrison<sup>60</sup> is in complete accord with the idea that "the augmented and accelerated action of the emotional heart ought also to lead to few rejections."

5. *Toxic*. Thirty-six cases of tachycardia, apparently due to intoxication of some kind, are grouped here. Some of these men were suffering from tonsillitis or some other mild infection at the time of the examination. Some were smoking an excessive number of cigarettes a day—thirty to sixty. Some few were alcoholic. Some were drinking enormous quantities of coffee. All of them had a rapid heart, apparently the result of some toxin, whether bacterial or a drug. Cases of tuberculosis or other severe infection with the associated tachycardia are

<sup>59</sup> The Recruit's Heart, British Med. Jour., October 16, 1915, p. 563.

<sup>60</sup> Ibid., October 30, 1915, p. 636.

not grouped here. Except for the rapid heart, physical examination disclosed nothing of moment. As regards effects of cigarette-smoking and alcohol there is of course considerable divergence of opinion.

Cigarette-smoking undoubtedly has the effect of increasing the heart action, but that it has any more serious effect is dubious. J. Parkinson and H. Koefid,<sup>61</sup> in a recent article in which the effect of cigarette-smoking is fully discussed, conclude that the smoking of a cigarette by habitual smokers raises the pulse rate, which effect is more pronounced in cases of soldier's heart; that excessive smoking is not the essential cause in most cases, but in their opinion it is an important contributory factor in the breathlessness and precordial pain of many of them. R. D. Rudolf<sup>62</sup> says that the excessive use of tobacco is often stated to be a cause of soldier's heart, and no doubt in many cases it is one. Lewis, however, does not lay much stress on tobacco as a cause of disordered action of the heart. In his series 5 per cent. did not smoke, and he calls attention to the fact that the same symptoms appear in soldiers who do not smoke. Likewise with alcohol, more than half of his cases were not consumers of alcoholic drinks and many of them showed actual distaste for it. Parkinson<sup>63</sup> found in his series of 40 cases that about half either smoked a pipe or were very light smokers, and that in regard to alcohol only 3 had been heavy drinkers. E. K. Tullidge<sup>64</sup> in his experience in Austrian service says that in a number of cases the disturbance could be traced directly to the excessive use of tobacco.

Fourteen cases of rapid hearts were seen which fell into no category. It was apparently impossible to group them satisfactorily.

SUMMARY. "Soldier's heart" is discussed in the light of the experience of our allies. The importance of tachycardia as a prominent and important objective symptom in the examination of the recruit is called attention to and a classification for cases of tachycardia is suggested.

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## NECROPSY SERVICE IN A MILITARY HOSPITAL IN THE FIELD.

By HOWARD T. KARSNER, M.D.,

CAPTAIN, M. R. C., U. S. ARMY, FRANCE.

THE following report is offered not because of its statistical value but because it represents fairly well the type of work a pathologist sees in a base hospital in France and because it offers certain suggestions as to the sequences and treatment of war wounds. It represents eight months' service in a base hospital in France of about 1250 beds. The total number of necropsies is 87, which represents nearly all the deaths that occurred in the period mentioned. The necropsies were performed under fairly satisfactory conditions, and, as a rule, a few hours after death. There were no limits as to the extent of the examination,

<sup>61</sup> The Immediate Effect of Cigarette Smoking on Healthy Men and on Cases of Soldier's Heart, *Lancet*, London, August 18, 1917, p. 232.

<sup>62</sup> Canadian Med. Assn. Jour., 1916, vi, 796.

<sup>63</sup> *Loc. cit.*

<sup>64</sup> The Heart of the Recruit and the Soldier, *Military Surgeon*, 1917, xl, 24.

and bacteriological examinations were made in all cases. The finer differentiation of bacteria was not possible because of limitations of time and staff. The study of anaërobes was difficult, and the results given are to be regarded as approximations rather than as accurate diagnoses of the anaërobes. For this purpose the primary culture was made in a medium recommended by Hibler and by Muriel Robertson, composed of lean beef, and water, equal parts, rendered slightly alkaline to litmus, tubed and autoclaved. A final estimation of the cause of death was not possible in some of the more complicated cases, and the cause assigned was that dictated by a consideration of the clinical and pathological aspects of the case.

Probably the most important phase of this report is the problem of dissemination of infection. Most of the war wounds contain several different organisms, and there appeared to be no explanation for the fact that in some cases the anaërobes are the most important for the patient, and that in other cases different forms of aërobes do the most damage. There were 28 cases in which streptococci were isolated from the heart's blood after death. Of these 2 were regarded as streptococcus pyemias, meaning metastatic suppurations in more than one position. The remainder are regarded as septicemias, although not all of them showed clinical symptoms. The technic of the heart cultures was very carefully controlled, and there is little likelihood that the organisms were contaminations; but there is always to be considered the possibility that they may have entered during the agony or after death. The cultures were pure except for 2 cases, in which *Staphylococcus pyogenes aureus* was also present and 5 in which an anaërobe was present as the result of gas gangrene, 4 being *perfringens* and 1 a motile organism, probably malignant edema. Only 1 case, a buttock wound, showed a demonstrable thrombophlebitis. Ten were cases of deep muscle wounds sometimes associated with bone injuries. Three followed penetrating head wounds, 3 penetrating pelvis wounds, 4 penetrating chest wounds and 9 followed wounds of the joints. Of these last 5 were of the knee-joint alone, 1 of knee and ankle, 1 of knee and elbow, 1 of hip alone and 1 of ankle alone. The seriousness of wounds involving the joints has been repeatedly emphasized by the surgeons, and much has been said and written about their treatment. This study can present no figures as to the frequency of septicemia as a complication, but does serve to draw attention to its importance, and any consideration of treatment must include this possibility. Attempts to save members, the joints of which are the seat of infection, must be most carefully guarded by close study of the case, and refractory cases should be subjected to most radical treatment, preferably amputation. There were 2 cases of pyemia due to *Streptococcus pyogenes*, 1 with large wound of buttock, fibrinous pleurisy and septic infarcts of the lungs and acute tricuspid valvulitis, 1 with penetrating wound of the pelvis, acute fibrinous pleurisy and septic infarcts of the lungs.

There were 7 cases in which *Staphylococcus pyogenes aureus* was isolated from the heart's blood; 3 of these were pyemias and 4 septicemias. In none of these were there wounds of joints, although 2 of the septicemias originated in chest wounds and 1 each of the pyemias and septicemias originated in penetrating wounds of the pelvis.



In addition to these septic cases there were 2 which were clinically and pathologically septicemic, but which were not identified bacteriologically because of faulty technic. There was 1 case of acute purulent meningitis due to *Streptococcus pyogenes* and apparently metastatic from an arm wound, although there was no growth in cultures from the heart's blood. Thirteen of the septic cases showed an acute valvular endocarditis; this matter, however, will be made the subject of a separate report. Of the 37 septic cases 27 showed spleens that were more than 150 grams in weight. There were 14 cases in which the liver weighed more than 2000 grams; 2 of these were not associated with enlargement of the spleen. The kidneys together weighed more than 300 grams in 21 cases, in 19 of which there was associated enlargement of the liver and spleen and in 2 there was associated enlargement of the liver only. Of the 37 cases only 5 failed to show parenchymatous change in the liver or kidneys or acute splenic hyperplasia. Of these 5 cases 4 were bacteriologically streptococcus septicemias and 1 was classed as a pyemia on the basis of gross morbid anatomy, but without bacteriological proof.

There were 17 cases of gas gangrene. Two of these died before the laboratory was equipped for satisfactory anaërobic work. Of the remaining 15 the heart's blood contained in 8 cases *Bacillus welchii*, in 2 cases a motile organism, believed to be the bacillus of malignant edema, and in 5 cases there was no growth. Of the cases showing organisms in the blood, the blood and tissues showed the usual foamy characters in all but one instance. Of the 5 showing no growth the organs and blood showed foamy change in 2 cases. In a general way it may be said that the cases reported "no growth" were sectioned earlier than those showing organisms, but one of the malignant edema cases was sectioned four hours after death and showed foamy organs. Most of the wounds were large deep wounds, 9 cases being thigh wounds, 3 of buttocks and pelvis (only one penetrating the gut), 3 arm and shoulder, 1 of the foot and 1 following an appendectomy; 5 of the cases were accompanied by a streptococcus septicemia. There are no particular notes to be made on the gross morbid anatomy of these cases, as the changes are well known and are modified in the usual way by the atmospheric temperature and the number of hours elapsed between death and autopsy. The cases were ill from three to fourteen days, the average being seven days. The average is raised by 2 twelve-day and 1 fourteen-day case, 4 being sick seven days and 7 being sick five days or less.

There were 12 cases of penetrating wounds of the chest. Most of these were studied bacteriologically before death by daily punctures of the chest. Frequently such punctures were sterile until four or five days after the wound had been inflicted, and such findings are common also in the non-fatal cases. Two of the cases should properly be classed as deaths from hemorrhage, one a hemorrhage into the chest following evacuation of a large amount of blood from the chest, the other showing frequent hemoptysis from a perforation of a branch of the pulmonary vein about 3 mm. in caliber. All but 2 cases showed a marked pleurisy, the 2 exceptions being cases of extensive old fibrous adhesive pleurisy, and 1 of these was a case that died of hemoptysis. Of the other 10 cases which showed acute pleurisy 9 had a bilateral involvement; 1 case showed also acute serofibrinous pericarditis; 5 cases had pene-

trating wounds of the lung and a bronchopneumonia; 1 of these showed also a most extensive acute interstitial pneumonia. Of the 7 cases without penetration of the lungs, 5 showed bronchopneumonia; 2 cases showed streptococcus in the heart's blood and 1 showed Staphylococcus pyogenes aureus. The fluid in the chests frequently showed the common wound flora, and a smear of the fluid, as a rule, could not be differentiated from a smear from a large superficial wound. In 1 of the cases Bacillus welchii was found in the heart's blood, although there was no foam in the blood and no evidence of gas gangrene. Most of these cases were ill about a week, but 1 was ill sixteen days, 1 ill twenty-one days and 1 ill twenty-seven days. The last showed a staphylococcus septicemia. The 2 streptococcus septicemias were ill nine and ten days respectively.

There were 9 cases of penetrating wounds of the head. These were all cases with penetration of the dura, but varied from cases with penetration of small pieces of shell or shrapnel to massive brain injuries with 3 cases of hernia cerebri. Six cases showed acute purulent basal meningitis, in 2 of which there was extension to the spinal meninges. In 3 of these cases, including the 2 with spinal involvement, there was pus in the ventricles. One other case showed an acute internal hydrocephalus associated with thrombosis of the lateral sinus, but no other evidence of infection. One case with basal meningitis and large wound of brain (tank rivet) showed extensive hemorrhage into the ventricles. Two cases died apparently of extensive subdural hemorrhage without real evidence of infection. None of the cases showed a septicemia. Five of the cases had been ill from two to nine days; 1 was ill twenty-eight days and died of meningitis; 1 was ill thirty-seven days and died of acute internal hydrocephalus; 2 cases which died respectively of brain abscess and meningitis lived forty and forty-five days.

There were 3 cases of penetrating wound of the spine. In one of these (sick nine days) there was fracture of the third lumbar vertebra, with hemorrhage in the pia arachnoid, but no suppuration. There was paralysis and anesthesia of the right leg and incontinence of retention, with acute hemorrhagic cystitis. Another case was sick four days and showed a shrapnel fragment embedded in the fourth thoracic vertebral body, severing the cord almost completely, with slight local purulent meningitis; there was a paraplegia and a most severe hemorrhagic cystitis. The third case, which lived twenty days, showed a small free shell fragment at the tenth thoracic region, with a profuse purulent inflammation of the membranes of the cord, the entire brain and the ventricles of the brain. There was no paralysis and no cystitis. None of the cases showed a septicemia, although the last case had had streptococci in his spinal fluid for more than ten days.

There were 9 cases of death apparently from hemorrhage; 6 of these had had more than 1 hemorrhage. Three of the latter group were chest wounds with penetration of the lung, one showing in addition a streptococcus septicemia. Of the 6 other cases the hemorrhage followed a wound of the pelvis in 1 and wounds of the lower extremity in 5 others; 2 of these 6 cases showed a streptococcus septicemia; 4 had been transfused without reaction, 2 cases once each, 1 case twice and 1 case three times. Of the total of 9 cases the spleen was enlarged in only 3, 2 of these having had a single transfusion, the other having had no transfusion but being a subject of a streptococcus septicemia. The bone

marrow was normal. The case which had had two transfusions had been sick twelve days, was a streptococcus septicemia and had a spleen slightly enlarged (180 grams), but otherwise normal. The case which had had three transfusions had been ill sixty-nine days with an enormous buttock wound, was not septicemic and showed a soft spleen weighing 120 grams. The general results found in this series of cases was to the effect that transfusion with matched bloods shows little effect from the view-point of gross morbid anatomy. From the clinical and pathological observations it was decided that wounds of deep vessels in the thigh and about the knee were often so obscured by the depth and the infection and the irregularity of the wound that unless the hemorrhage after careful dissection and examination could be completely stopped the surgeon must consider the advisability of amputation for the purpose of controlling the bleeding. In civil surgery this might seem extremely radical, but the conditions of military surgery sometimes make it necessary.

In addition to the 9 foregoing cases of hemorrhage there were 3 of hemorrhage complicated by transfusion reactions. The first was a shell wound of the pelvis with repeated hemorrhage, which after a transfusion developed chills and cyanosis and died in a few hours. There was no hemoglobinuria, and the spleen aside from weight (160 grams) appeared to be normal. The second case had two transfusions following a single large hemorrhage from a shell wound of the pelvis, the second transfusion through a confusion of names resulting in the use of a group 2 donor for a group 4 recipient. At necropsy there was found a firm enlarged spleen (360 grams) hemoglobinuria, normal bone marrow and a streptococcus septicemia. The third case had 1 transfusion for a large hemorrhage from a shell wound involving the popliteal artery; there was immediate reaction followed in a few hours by death, and it was afterward found that a group 3 donor had been used for a group 2 recipient. There was no hemoglobinuria and the bone marrow was normal, but the spleen weighed 170 grams, was tense and showed numerous small hemorrhagic infarcts. This patient had been ill for twenty days and was clinically a case of septicemia, but cultures from the heart's blood at autopsy showed no growth.

There were 4 deaths following "mustard-gas" poisoning, an extremely irritant gas  $(CH_2)_4Cl_2S$ , which was first used by the German army in the summer of 1917. One of these showed a mild bronchopneumonia and suffered also from a Staphylococcus aureus septicemia following a shell wound of the pelvis. The other 3 cases had no wounds. They all showed skin burns of varying degree. The necropsies showed a dusky red congestion of all the viscera, including in 2 cases the brain, accompanied in the stomach by submucous petechiae in the fundus. The conjunctiva and the membranes of the nose and pharynx were the seat of a marked mucous inflammation. The larynx, trachea and bronchi showed severe inflammation, in 1 case accompanied by pseudomembrane formation and in the other 2 with extensive necrosis of the mucosa, with multiple ulcers from 1 to 3 mm. in diameter. Two of the three showed acute fibrinous pleurisy. All showed a bilateral bronchopneumonia, with slight general edema of the lungs. The pneumonic patches were irregularly distributed, and varied in size from

2 mm. to 3 cm. in diameter, reddish gray or gray in color, solid, projecting in the cut surface, moist but finely granular.

Of the miscellaneous cases not justifying special description were 1 each of multiple pulmonary embolism, fat embolism, diabetes mellitus, malignant endocarditis (non-surgical), insufflation pneumonia following a traumatic tracheo-esophageal fistula, acute dilatation of the stomach in a case of congenital aplasia of the jejunum, ileum and colon.

It will be noted that in the eight months' service, from May 25 to January 25, there were no deaths from lobar pneumonia, although bronchitis and bronchopneumonia were of very frequent occurrence. There was no case of active pulmonary tuberculosis, although 10 cases showed the so-called healed lesions, small caseous or calcified areas surrounded by fibrous connective tissue. In addition to these cases there were 18 cases of chronic adhesive pleurisy without any evidence of tuberculosis to the ordinary careful gross examination. Of these, 10 were apical adhesions, 4 basal and 4 extensive, involving practically the entire pleura.

In passing from civil life to work in an active military hospital in the field the medical officer is beset by many difficulties and must readjust his point of view in regard to many things. The above series of necropsies was found to be of value in several respects. The results served to alter the surgical treatment of wounds of the extremities, particularly those involving joints to a considerable degree. In place of the conservative surgery of civil life which permitted in the badly infected war wounds the possibility of a septicemia, with its incident effects on internal viscera, there developed a more radical surgery which, although it might sacrifice a limb, assured the patient of survival with little chance of damage to important viscera. In regard to hemorrhage the postmortem examination of wounds showed the possibility of large vessels being wounded in such a way as to escape detection even with most careful operative dissection. This led to several amputations for the complete control of hemorrhage, undoubtedly to the advantage of the patients. Deaths from transfusion with antagonistic blood, which the necropsy showed to be largely due to the transfusion reaction and not to other causes, led to a firmer insistence on careful testing of the bloods before transfusion. It is believed that this is even more important, if possible, at the base where patients may have been drained by infection for days or weeks than in the hospitals near the front, as has been indicated in another paper.<sup>1</sup> The accurate diagnosis of cases permitted by postmortem examinations is undoubtedly an aid in the adjustment of pension and insurance claims as well as statistical value in the army medical service. With all these points in view it is urged that postmortem examinations should be established as a routine procedure because of their unquestioned value to the soldier, to the army and to the nation.

<sup>1</sup> Jour. Am. Med. Assn., 1918, lxx, No. 77, p. 769.

## REVIEWS

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MEDICAL WAR MANUAL, No. 2. NOTES FOR ARMY MEDICAL OFFICERS. By LIEUT.-COL. T. H. GOODWIN, R. A. M. C. Pp. 112; 33 illustrations. Philadelphia and New York: Lea & Febiger.

ANY American medical officer who fails to read this little book neglects an opportunity to add to his efficiency. The distinguished author of this manual, Colonel Goodwin, of the British Royal Army Medical Corps, understands the medical problems of the European battlefields as few men do. In the brief compass of this book he has summarized his long experience at the front and has answered most of the troublesome questions that confront every American medical officer anticipating active duty with our troops in France.

The book is divided into three sections: The first part deals with the organization of the British medical service and the duties performed by its various officers and units. A useful comparison has been drawn between our own medical department and that of our English ally. The chapter furnishes a definite idea of just what is required of medical officers from the battalion surgeon, serving with troops in the trenches, back to the large groups of specialists working in the stationary hospitals in the rear.

The second part of the book takes up war surgery. Obviously it would be impossible in a work of this type to treat so broad a subject exhaustively. Colonel Goodwin's object evidently has been to emphasize the salient points, the fundamental principles that must never be lost sight of if the wounded are to be successfully handled. He has attained his purpose. To read this chapter is to have one's perspective properly adjusted so as to see more clearly the essential difference that exists between civil and military surgery. The account of the emergency handling of fractures is especially noteworthy.

The concluding section of the book on sanitation in war is of unusual interest and importance. In it the author discusses such vital problems as the disposal of excreta and waste in the zone of the advance, the protection of water supplies, the destruction of lice and flies, the management of divisional baths, the disinfection of clothing, and the control of infectious diseases.

From cover to cover the book is full of valuable information, presented with unusual interest, and arranged in a convenient form for ready reference. Like all the war manuals in this series its size admits of the book being easily carried in the pocket of any uniform. It is decidedly the most generally useful work of its kind that has appeared and it undoubtedly deserves a place in the armamentarium of every medical officer.

G. M. P.

MILITARY OPHTHALMIC SURGERY. By ALLEN GREENWOOD, M.D., GEORGE E. DE SCHWEINITZ, M.D., and WALTER R. PARKER, M.D. Philadelphia: Lea & Febiger.

THIS small brochure deals with military surgery, trachoma and acute conjunctival infections and the best methods for the detection of malingerers.

Greenwood has spent some time in base hospital work back of the Allied lines. He is the author of the chapter on surgery. He emphasizes the importance of skilled ophthalmic examinations and points out the ease of overlooking important ocular lesions in the presence of other devastating bodily injuries.

Two interesting measures advocated are the more general use of glass balls or other material implanted following enucleation and some form of suction apparatus in traumatic cataract.

In 4 out of 5 cases of orbital cellulitis Carrell's tubes proved efficient.

The chapter on trachoma and conjunctivitis by de Schweinitz is in that author's characteristic and authoritative style.

Of great value to the draft board examiner is the last chapter on malingerers and their detection.

This brief work should be carefully studied by all men whose medical duties will summon them to cantonments or back of the fighting lines.

B. F. B.

AMERICAN ADDRESSES ON WAR SURGERY. By SIR BERKELEY MOYNIHAN, C.B., Temporary Colonel, A. M. S., Consulting Surgeon, Northern Command. Pp. 143; Philadelphia and London: W. B. Saunders Company.

THESE addresses or papers were read in Chicago or elsewhere during the author's recent visit to this country. The subjects are as follows: The causes of the war; gunshot wounds and their treatment; wounds of the knee-joint; injuries to the peripheral nerves and their treatment; gunshot wounds of the lung and pleura. It

was the reviewer's privilege to hear the author deliver the first address, which was a very impressive occasion. All the subjects are handled in the same clear, direct and forcible style. None can be more important to the war surgeon than gunshot wounds and their treatment. In this paper we have a master surgeon, after abundant war experience, laying before us briefly and clearly the various new methods of treatment which have gained recognition during the war and his judgment as to their relative values. In like manner we are treated to a most instructive digest of the work done and the important results obtained in connection with the other conditions discussed. How interesting it is to learn, after all our fears concerning and our efforts to prevent collapse of the lung when the chest is opened, that the thorax is being opened widely, the collapsed lung being delivered, the wounds in it being sewed up as in other tissues, the repaired lung being replaced in the chest and the thoracic opening tightly closed, with a wonderful improvement in the results over those of previous methods of treatment.

T. T. T.

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PUBLICATIONS OF THE RED CROSS INSTITUTE FOR CRIPPLED AND  
DISABLED MEN. A BIBLIOGRAPHY OF THE WAR CRIPPLE.  
Edited by DOUGLAS C. McMurtrie.

THIS recently published and up-to-date *Bibliography of the War Cripple* is of timely interest and should prove of great value to students of the subject and to the increasing number of workers in this important field. There is comprised in it a list of references to literature pertaining to the reëducation, employment and other forms of care of crippled soldiers and sailors. The compiler of this bibliography takes pains to make clear that whereas every effort has been made to make it as full as possible within the particular field covered, there have been purposely excluded articles dealing solely with medical or surgical subjects, with the pension system and with provision for the blind, the deaf and the nervously deranged. While the importance of these subjects is recognized, it is felt that they fall outside of the limited scope of this index.

It is stated that practically every entry has been made from the original publications. It is further stated that nearly all the indexed literature is reproduced in either the private library of the compiler or the collection of the Red Cross Institute. Both of these collections can be consulted at the library of the Red Cross Institute for Crippled and Disabled Men, 311 Fifth Avenue, New York City. A survey of the titles included in the present publication indicates that most of them are from Continental sources, French and German equally, the balance being made up of English and a few Italian contributions. Provision will be made for current accessions of material along these lines by issuing supplements to the present list.

R. P.

**FUTURE OF THE DISABLED SOLDIER.** By C. W. HUTT, M.A., M.D., D.P.H., Oxford Deputy Medical Officer of Health, County Borough of Brighton; Recently Member of Brighton War Pensions Committee. New York: William Wood & Co.

THIS excellent little book of but 200 pages gives a fund of information regarding the experiences of Great Britain, France and Germany in the matter of reëducing the partially disabled soldier and training him to be an independent member of society. Our problem in this country is going to be very soon brought to our notice and it will do well for all industrial physicians and managers of employment departments of our large industries to study carefully the pages of this book.

The first chapter deals with the arrangements for treatment; then follows chapters on the training of the disabled in the several countries and lastly a chapter on the employment of the disabled.

The opinion seems to prevail that many lines of training should be carried out in trade schools, taking groups of disabled men, rather than encouraging employment in ordinary workshops where the disabled would have to compare himself with able workmen with resulting discouragement. It is also pointed out that the earlier the attempt to induce men to take up training the better, and that whenever possible disabled men undergoing training should be used to convert others.

The general experience is that the men do not avail themselves to the extent that they should of the opportunities placed at their disposal for learning skilled trades. The causes of this disinclination are discussed and remedies suggested.

At the end there is a useful appendix tabulating occupations suitable for defectives.

C. N. S.

**THE SURGICAL OPERATIONS ON PRESIDENT CLEVELAND IN 1893.**

By MAJOR W. W. KEEN, M.R.C., Emeritus Professor of Surgery, Jefferson Medical College. Pp. 52. Philadelphia: George W. Jacobs & Co.

It is fortunate that even at this late date such important historical events as are related in this small volume are now placed on record by one of the principal persons concerned in them. That events of such importance to the public could have escaped the press is marvelous. They are now recorded here and fortified by the notes of those men most responsible in the performance of the operations.

T. T. T.



# PROGRESS OF MEDICAL SCIENCE

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## SURGERY

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UNDER THE CHARGE OF

T. TURNER THOMAS, M.D.,

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UNIVERSITY OF PENNSYLVANIA; SURGEON TO THE PHILADELPHIA GENERAL  
HOSPITAL AND ASSISTANT SURGEON TO THE UNIVERSITY HOSPITAL.

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**Carcinoma of the Splenic Flexure of the Colon.**—HARTWELL (*Ann. Surg.*, 1917, lxvi) presents a report of 6 cases and a study of the literature. He says that the splenic flexure of the colon is the third most common site for colonic cancer. This growth tends to the production of obstruction, with indeterminate premonitory symptoms. This complication occurs acutely in nearly three-fourths of the cases coming to operation. A recognition of the foregoing facts and a more careful detailed study, with a possible exploratory operation, should lead to an early diagnosis in a majority of the cases and thus forestall acute complications. The probable operative mortality of all cases up to the present time is over 60 per cent., and the percentage of the prolonged cures is exceedingly low, 10 per cent. to 25 per cent. These appalling results are largely due to the delayed diagnosis, and an improper mode of attack. The latter should follow the principle of the two or more stage operation, with provision for external colonic drainage, either as a preliminary, or at the time of resection; always the former in the presence of serious obstruction or abscess formation. The distal portion of the transverse colon, the flexure, and the entire descending colon must be resected in order to obtain the requisite conditions for a secure anastomosis with an ultimate patency of the colonic lumen. Notwithstanding the meager success thus far obtained, attention to the lessons learned from the successes and failures of those who have worked in this field justifies the hope that this lesion may be as satisfactorily dealt with as cancer in other parts of the body.

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**Pituitary Gland and Generative Organs.**—GOETSCH (*Surg., Gynec. and Obst.*, 1917, xxv, 229) says there is a close interrelationship in function between the pituitary and sex glands, a fact supported by abundant experimental evidence and by numerous observations on pituitary disturbances in the human subject. Overfunction of the pituitary anterior lobe is associated with overactivity of the sex glands. Deficiency of pituitary secretion in the individual is followed by under-

development and genital aplasia in the young and by sexual inactivity and retrogression in the adult. Primary alterations of function of the sex glands, as in pregnancy and after castration, are followed by pituitary hyperplasia and hypertrophy. The specific action of posterior lobe extract ("puititrin," "pituitary liquid") upon the smooth musculature of the uterus and bowel has led to the wide usage of this drug in obstetrical practice and in the treatment of intestinal paresis following abdominal operations. The administration of pituitary extracts is of distinct benefit in clinical states of pituitary underfunction.

**The Physiological and Pathological Importance of the Parathyroid Gland from the Experimental Aspect.**—VOEGLIN (*Surg., Gynec. and Obstet.*, 1917, xxv, 244) says that the parathyroid gland has a definite physiological function which is still incompletely understood. The presence of a minimum of parathyroid tissue in the body is essential for life and the continuation of normal metabolism. Parathyroid insufficiency seems to be characterized by an increased irritability of the nervous system to the galvanic current, which may be due to the withdrawal of soluble calcium salts from the blood and tissues. Parathyroid insufficiency leads to an alkalosis which is converted into an acidosis as a result of active tetany. Definite metabolic changes take place in animals after complete parathyroidectomy. Pregnancy puts an extra strain on the functions of the parathyroid, as evidenced by the appearance of tetany during this period in partially thyroidectomized animals. Tetany has been observed during lactation in animals with parathyroid insufficiency. Interruption of lactation was followed by recovery. The offspring of partially parathyroidectomized animals exhibit a marked increase in nerve irritability. An intravenous injection of soluble calcium or strontium salts or hydrochloric acid almost instantly removes the symptoms of tetany. However, tetany may reappear after this treatment and the life of such animals cannot be saved by the continued administration of calcium. The injection of parathyroid extract seems to have a temporary curative effect on tetany animals. Isotransplantation of parathyroids into animals with parathyroid insufficiency is usually successful. The spontaneous recovery from tetany in experimental animals is probably due to changes in their metabolism (acidosis) caused by the hyperactivity of the skeletal muscles during tetany. The experimental facts do not support the theory that eclampsia is due to hypoparathyroidism. A condition which might justly be termed hyperparathyroidism is known at the present time.

**The Pineal Gland.**—McCord (*Surg., Gynec. and Obst.*, 1917, xxv, 250) says that a clinical syndrome is to be associated with disturbances of the functions of the pineal gland. Because of the involution of the pineal at puberty, the constitutional manifestations of pineal pathology appear to be confined to prepuberal years. The essential characteristics (apart from pressure and neighborhood manifestations) are (a) early sexual development evidenced in the enlarged genitalia, pubic hair, general body hair, early change in voice; (b) precocious mental development, manifested in maturity of thought and speech; (c) general overgrowth of body to the extent that a child of six or seven years may

have the appearance of a child near puberty. The experimental extirpation of the pineal gland is surgically possible. The gland is not essential for the maintenance of life. The early symptoms following pinealectomy are attributable to the severe brain injury. No changes attend the removal of the gland in adult animals. As to the effect of pinealectomy in young animals, Sarteschi, Foa and Horrax respectively state that the removal of the gland leads to precocity of development. Exner and Boese and Dandy report no change after pinealectomy. The administration of pineal substance to young mammals is reported to hasten growth and sexual maturity. In unicellular organisms (paramecia) pineal extracts increase the rate of reproduction to more than double that of controls. In larval forms (ranidae) both growth and differentiation are hastened as a result of pineal feeding. The inference is allowable that the pineal gland is an organ of internal secretion whose functions, however, are of minor significance in the general activities of the endocrinous system.

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**The Endocrine Function of the Pancreas and its Relation to the Sex Life of Women.**—CARLSON (*Surg., Gynec. and Obst.*, 1917, xxv, 283) says that all evidence supports the view that some substance or hormone secreted by the islands of Langerhans into the blood is necessary for utilization of sugar by the tissues. This function is specific for the pancreas. Other endocrine organs may influence sugar metabolism in a superficial way by altering the sugar mobilization (adrenals, thyroid) or by increasing or decreasing the rate of oxidation in the body general. The rest of the endocrine glands cannot maintain the power of the tissues to oxidize sugar in the absence of the pancreas, and the hypoactivity or hyperactivity of other endocrine glands do not produce actual diabetes in the presence of a normal pancreas. While the failure of the tissues to use sugar in the absence of the pancreas is the central and definitely established fact, there are probably other primary defects in the development of acidosis, lipemia, increased metabolism, lowered resistance to infection, etc. All the evidence points to the view that true diabetes mellitus in man is primarily the result of pancreatic deficiency (islets). There is, at present, no evidence of any specific relations of the endocrine functions of the pancreas to the gonads, male or female, or to menstruation, pregnancy, and lactation. Absolute diabetes induced after conception leads to death of the fetus. Absolute diabetes probably renders conception impossible. Partial diabetes under careful dietary control permits of normal sex life of women (menstruation, normal pregnancy, normal child, lactation), and pregnancy under such conditions does not aggravate the diabetes. But in the absence of such dietary control the pregnancy aggravates the diabetes in the mother, and uncontrolled diabetes in the mother is extremely injurious to the fetus. There is some evidence that in the late stages of pregnancy the fetal pancreas may function for the mother.

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**The Surgery of Bronchiectasis.**—ROBINSON (*Surg., Gynec. and Obst.*, 1917, xxiv, 194) reports five complete resections of the lower lobe of the lung, with one death. Bronchiectasis is a chronic loathsome disease—generally regarded as incurable. The expectoration is disgustingly

profuse; consequently the afflicted loses employment, shuns society, becomes a recluse and not infrequently resorts to dissipation. He is pale and a trifle cyanotic. His fingers and toes are clubbed. He labors with early fatigue. He coughs spasmodically with varying persistency. Stooping, laughing, eating, hurrying, flood his trachea with pus and he retires, embarrassed, to drain himself of abundant sputum. In winter he is periodically ill with severe "colds" sometimes with bronchopneumonia, nor does the mildness of summer rid him of chronic cough. He may live many years until cerebral abscess, pneumonia, septicemia, amyloid disease, or hemorrhage happily ends his existence. Advanced bronchiectasis cannot be cured by medication, inhalations, intra-tracheal injections, intratracheal irrigations, climatotherapy or vaccines. Collapse therapy produced either by nitrogen, artificial pneumothorax or by surgical measures is not curative. Pulmonary arterial ligation is of more definite value as a preparation for lobectomy than as a curative measure *per se*. Excision of the diseased portion of one lung is the only curative treatment of advanced bronchiectasis. In the present status of the development of thoracic surgery, lung resections should be performed in two stages or three stages. The several-stage operation of the rib-resection type has been attended in the writer's experience with a 20 per cent. mortality. The operation of intercostal lobectomy has distinct technical advantages. When performed in one stage, an undue risk of life is incurred. The physiological advantages of the several-stage technic may yet be successfully combined with the technical advantages of the intercostal exposure.

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## THERAPEUTICS

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UNDER THE CHARGE OF

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**Nephritis from the Stand-point of Urea Excretion.**—McLEAN (*Jour. Am. Med. Assn.*, 1917, lxi, 437) attempts to make clear what actually happens in the condition of urea retention. Urea retention in the sense in which the term is now generally used is not a continuous process of piling up of urea in the blood, due to inability of the kidneys to excrete the large amounts of urea formed in the body, but is applied to any condition associated with an abnormally high concentration of urea in the blood and is taken to indicate disturbed renal function. The kidneys may be able to excrete far greater amounts of urea than they are ordinarily called on to do, even in severe cases of nephritis, while the condition known as urea retention exists in these cases at the lower levels of protein metabolism just as it does at the higher, even though in the former instance the blood urea figure may be within normal limits. McLean reviews briefly the classic work of Widai and Javal

and of Ambard and Weil, and then proceeds to report his own findings in 2 patients suffering from chronic nephritis. Both patients bore the strict dietary regimen well and showed no change in general condition at the end of the experiment, and are still alive a year after the conclusion of the investigation. Because of the length of the experiment the diet was varied more than is usual in metabolism experiments, but analysis was made of all protein-containing food. The intake of fluid and of chloride was kept constant. Twenty-four-hour specimens of stool and urine were analyzed daily for nitrogen. Blood-urea determination and a simultaneous urine analysis on a timed specimen were made twice a week to compute the index of urea excretion. Both cases are exactly similar and show the essential features described by Widal and Javal in their case; that is, a close parallelism between nitrogen intake, concentration of urea in the blood and nitrogen output. A change in nitrogen intake was always quickly followed by a change in the concentration of urea in the blood and in nitrogen output, so that nitrogen balance was reestablished on a new level. Variations in the diet increased the urea concentration of the blood from 0.262 gram per liter to 2.542. This latter figure is far above the level at which Hewlett, Gilbert and Wickett believe that toxic effects of urea appear, yet McLean's patient showed no uremic symptoms. The findings regarding urea excretion are of special interest: In Case I, with a variation in blood urea from 0.211 gram per liter to 0.855, the index of urea excretion remained remarkably constant, with an average of 21.4. In Case II there is a greater range of variation, the most significant being present when the blood urea reached 2.542 grams per liter. On that day the urea index was 8.3 instead of about 20. This would seem to indicate that here the maximum capacity of the kidney to excrete urea had been exceeded and actual accumulation had begun. This occurred only when the nitrogen intake had been maintained at over 36 grams per day for two days. The 2 cases confirm the findings of Widal and Javal and add the fact that no essential variation in the ability of the concentration of urea in the blood at various levels of protein metabolism was demonstrable until a very high level was reached; that is, the quantitative relationship that existed between the concentration of urea in the blood and the rate of its excretion remained the same at all levels of protein metabolism. McLean believes that he has demonstrated that a relatively increased concentration of urea in the blood follows the increased resistance with which diseased kidneys oppose the passage of urea. When as the result of feeding an increased amount of nitrogen the concentration of urea in the blood rises a parallel increase in the rate of excretion of urea occurs. When a point is reached at which the rate of urea excretion is kept equal to the rate of formation by the organism the level of urea in the blood ceases to rise and the organism remains in nitrogen equilibrium. But when the nitrogen intake is diminished, urea is excreted for a time more rapidly than it is formed, until the level of blood urea falls and reaches a point such that the rate of urea excretion is again equal to the rate of urea formation and the organism is once more in N equilibrium. This is the explanation offered by McLean for the events occurring in the so-called retention of urea.

## OBSTETRICS

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UNDER THE CHARGE OF

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**A Comparison of the Principal Methods in Use at Present for Performing Cesarean Section.**—FERRONI (*Annali di Ostetricia*, No. 9, 1916) compares the principal methods now in use of performing Cesarean section. He traces the development of the transperitoneal method and draws his conclusions from a series of fifty-seven sections performed by different methods. These operations were done for contracted pelvis and where the mother was uninfected at the time of operation, good results were obtained. He believes that in the average case, the simple classic method is best, and in performing transperitoneal operation he uses the anterior incision only.

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**A Comparison of Induced Labor with Delivery by Cesarean Section.**—HOFMIER (*München. med. Wchnschr.*, August 11, 1916) compares the results of these two operations for eight years in his clinic at Würzburg. In this time there were 76 cases of premature labor and 73 Cesarean sections. In the total 149 cases there was one maternal death, a woman who had been subjected to manipulation and infected before admission to the clinic. The Cesarean operations were suprasymphysial and transperitoneal. The fetal mortality was the same after both operations. The Cesarean patients were convalescent in fifteen days on the average. Where the patient can be procured for operation before the membranes are ruptured the results of Cesarean operation are fully as good for the mother as those of induced labor, and hence the operation as a rule should be preferred.

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**Pain Over the Uterus.**—BEACH (*Am. Jour. Obst.*, August, 1916) describes the case of a woman in her second pregnancy, who had considerable pain over the uterus, and one week before term the patient noticed excessive movement on the part of the child. These were so violent as to prevent sleep. The movements soon became very much less violent and fetal life was still present. When labor began the signs of fetal life ceased with the first pain. The child was finally stillborn spontaneously, with eight coils of cord about the neck. The reviewer recalls the case of a multipara near term who slipped and fell upon a rug which slid from her feet on a highly polished floor. The mother was not much injured, as she struck upon the back. The fall produced little effect upon the mother, but she noticed that fetal movements became excessively violent and then became normal or less than normal. Labor developed and it was necessary to deliver by forceps. The cord was found coiled several times about the neck of the child. The child was asphyxiated and was revived with difficulty, but died of inspiration pneumonia. It seemed fair to believe that the fall had produced violent fetal movements in which the cord became coiled

about the body of the child and the traction upon the cord at birth interfered with the child's circulation and produced involuntary movements of respiration. Through these, material from the genital tract of the mother was drawn into the lungs and set up pneumonia. The reviewer had at one time under his care a primipara, with ample pelvis and fetus of moderate size, who failed to come into labor at the proper time. There was no attempt at engagement or descent. The patient was delivered by elective section and the umbilical cord was found twice around the neck, over each shoulder, and under each axilla. Spontaneous labor was impossible without separating the placenta, which would have immediately caused the death of the child, and threatened the mother with the dangers of concealed accidental hemorrhage. The life of the child was undoubtedly saved by the operation.

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**Brachial Birth Palsy.**—THOMAS (*Am. Jour. Obst.*, April, 1916) contributes a paper upon this subject and gives a summary of 11 cases. The paper is well illustrated by photographs. In cases in which there is no displacement of the shoulder-joint a perfect recovery will be obtained from exercise alone. The condition is considered of great importance, and is believed to be the result of trauma occurring during birth. As soon as possible, if there is dislocation, a complete reduction should be attempted, and whether reduction is complete or not, vigorous and prolonged exercise afterward will improve the motion in the joint. Reduction by non-operative methods calls for the application of such great force that it is exceedingly dangerous. In operation the joint is freely exposed, the deltoid divided from the upper end of the humerus, and the obstructing portion of the acromion is removed. This is usually cartilaginous and can be cut with a knife. Efforts should then be made to bring the arm to external rotation and abduction and the head of the humerus as nearly as possible in its normal position. It will often be impossible to accomplish complete reduction because of the traction of tendons and their tissues, but almost always considerable improvement can be obtained. It may be necessary to divide the insertion of the subscapularis before external rotation can be obtained. The wound is closed with continuous plain catgut sutures and a sterile gauze dressing applied with a light plaster cast.

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**Pyloric Obstruction in Infants Treated by Operation.**—DOWNES (*Surg., Gynec. and Obst.*, March, 1916) publishes a paper upon this subject in which he gives a summary of his experience in 66 cases observed in five and one-half years. With one exception there was the characteristic tumor at the pylorus, consisting of marked hypertrophy of the band of muscle fibers with thickened mucous membrane lying in longitudinal folds. In the one exception noted the baby died, and on autopsy a small tumor originating in the muscular mucous tissue was filling the lumen of the pylorus. Most of the stomachs were of average size, one so small that it would hold but one ounce. There was edema in varying degrees in all. The symptoms are projectile vomiting, tumor, peristaltic waves, gastric retention, and rapid loss of weight. Marked constipation is usually present, and a tumor can frequently be felt. In a previous series of 61 cases the mortality was 22 per cent. These were treated by gastro-enterostomy. This has been abandoned, and

Rammstedt's method has been given a thorough trial. In 19 done after this method a sound was passed through the pylorus after the muscle had been divided. The operation consisted in incising the tissues of the pylorus longitudinally down to the mucous membrane but not through it. The tissues are then stretched gently by the finger. Of partial pyloroplasties there were 8 deaths, a mortality of 23 per cent. The postoperative treatment consists in very careful and limited feeding, and usually something is given the child in about two hours after the operation. From 2 to 3 drams of breast milk, alternating with water, is selected. This is gradually increased until the child comes up to the normal standard. In favor of the operation is the fact that it is simple and that it permanently removes the obstacle.

**Enlarged Thymus in Infants.**—HERRICK (*Surg., Gynec. and Obst.*, March, 1916) describes 6 cases of enlarged thymus in infants, and calls attention to the difficulty in diagnosis between enlarged thymus and great enlargement of the mediastinal glands. In enlarged thymus the dulness is higher up with a notch between it and the heart area, whereas when dulness comes from enlarged glands it is near the bifurcation of the trachea and vessels. Examination by the x-rays will often assist. A thymus case is usually well nourished, but pale and pasty, with no tubercular history. A tubercular case may be reduced in flesh, less vigorous in appearance, and have slight elevation in temperature. As regards treatment, operation is dangerous and uncertain, and probably the x-ray is the most satisfactory method. Of the 6 cases, 3 recovered and 3 died. The x-ray treatment seemed successful and is the only treatment which could be safely employed in such frail patients.

**Obscure Fever in the Newborn.**—COPELAND (*Jour. Am. Med. Assn.*, November 4, 1916) finds that the nervous instability of infants is frequently a cause for considerable rise in temperature which may continue over varying periods. Such infants are apt to be rachitic and frequently show evidences of tetany, laryngismus, stridulus, and general convulsive seizures. Obscure inflammation of the middle ear is another cause for the development of fever. Obscure disease of the tonsils, even in very young children, may also be a cause. The paper emphasizes the necessity for careful examination in these cases.

**Influence of Syphilis on the Production of Children.**—HARMAN (*British Med. Jour.*, February 5, 1916) in studying 1100 children to ascertain the percentage of blindness, found 150 family histories in which syphilis appeared as a cause of congenital or inherited disease. In 68.5 per cent. of the blind children the Hutchinsonian teeth were present, and there were other symptoms in addition. In direct contrast with these are the histories of 150 families where it was known that syphilis was not present. The 150 syphilitic mothers had 1001 pregnancies, but of these only 390 resulted in the birth of fairly healthy children. On the other hand, the 150 healthy mothers had 826 pregnancies, and from these there resulted 654 healthy children. It is interesting to observe that the syphilitic mothers had 17 per cent. more pregnancies than the healthy mothers. This may be accounted for, at least in part, by the frequency of miscarriages and stillbirths in a syphilitic, and the



short interval between many of these would allow of several ineffective pregnancies in the same time that would be taken for one full-term pregnancy in a healthy mother. The results of these comparisons are sufficiently striking to indicate the great importance of syphilis in diminishing fertility.

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**Spontaneous Evolution during Labor in Shoulder Presentation.**—CARTER (*Surg., Gynec. and Obst.*, November, 1916) describes the case of a multipara whose previous labors had been successful, but in the one described had prolapse of an arm followed by cessation of active uterine contractions. On examination the left arm was prolapsed, the scapula anterior, and the arm was of good color. The cervix was fully dilated and the shoulder was firmly wedged into the pelvis. It was impossible, without using more force than was prudent, to carry the hand upward into the uterus to perform version. As the patient was not having hard pains and her general condition was good she was taken to the hospital in a motor car. This seemed to do her no special harm. A few moments after entering the hospital the pains increased in number and intensity, followed by violent bearing-down efforts at intervals of two or three minutes. She was immediately given a light anesthetic and placed upon the operating table. The prolapsed arm had now become very much swollen and congested and the shoulder had rotated beneath the pubis. The chest, abdomen, and breech were consecutively forced over the perineum. The head was extracted without difficulty and the placenta followed within five minutes. The child was dead, but death had evidently been very recent. The reviewer recalls the papers of the late Dr. King, of Washington, in which he described spontaneous evolution in shoulder presentation, transverse position, and recommends the squatting posture for the patient. In this the thigh of the mother nearest the fetal head was to be considerably advanced, and it was thought that by this manœuvre additional pressure was brought to bear upon the fetal head to force it upward so that the breech might come into the pelvis. He described several cases in which spontaneous evolution was successful. In the observation of the reviewer he was called on one occasion to a woman in active labor, finding a shoulder presentation, transverse position, and sent immediately for assistants for etherization. Before they arrived following two especially vigorous uterine contractions spontaneous evolution occurred and the child was expelled in breech presentation. In this instance the mother insisted upon squatting upon the floor by the side of her bed, inclining the trunk of the body forward and resting the weight of the head and shoulders upon the bed.

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**Migrating Phlebitis.**—HEDBLUM (*Jour. Am. Med. Assn.*, 1916, lvi, 1777) reports the case of a woman, aged twenty-eight years, in her fourth pregnancy occurring during five years. The first two children had died of exhaustion, the third was living and well. At the end of twelve hours a fairly developed child was spontaneously born. There was no laceration and the placenta came away spontaneously. The uterus did not contract well and there was more than the usual loss of blood. On the eleventh day of the puerperal period the patient had severe night-sweat followed by fever. The white blood corpuscles were

17,000; hemoglobin, 60 per cent. There was inflammation of the right saphenous vein which gradually subsided. This was followed by inflammation of the other veins in the left side of the neck, axilla, arm and chest. This subsided, to be succeeded by swelling in the other portions of the body. In all the patient had six relapses, each attended by more or less severe constitutional prostration. The patient finally recovered and was discharged in the nineteenth week in good general condition.

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## OTOLOGY

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UNDER THE CHARGE OF

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**Prevalence of Ear Injuries and Diseases in the French Army.**—BRYANT (*Jour. Laryngol., Rhinol. and Otol.*, vol. xxxii, No. 11). The importance of the inclusion of provision for the care of the war deaf in the United States is emphasized by the author. In his record of observations in the French service the number of cases of ear injuries and deafness exceeded those of other observers in the English or Italian services, the ear cases being nearly as numerous as the eye patients, although there have been more cases of total loss of function among the eye cases than among the ear cases, with correspondingly more rapid recoveries, and a larger proportion of cases of very considerable impairment of hearing than of sight, the proportion of ear cases to the total number of cases in the evacuation hospitals being 16 per cent., about 80 per cent. of all ear cases showing considerable impairment of function. The nature of the injuries and their complications are included in three categories: rupture of the sound-transmitting apparatus of the middle ear and its complications; suppuration, acute and chronic; mastoiditis; mastoid abscess and its sequence; injuries of the terminal nerve-ending apparatus, of which the cochlear branch is always the more vulnerable, these injuries being of sudden occurrence or gradual implication and due severally to the larger use of high explosives and the more continued effect of powerful detonation than has ever been previously experienced. As the result of the explosion of powerful shell mines, hand grenades, bombs and rifle explosives causing, in addition to rupture of the membrana tympani, hemorrhage, ecchymoses, and, luckily, limited disintegration of the sound-transmitting apparatus, there is, in consequence of long exposure to loud noise, interference with the nutrition and causation of microscopic changes in the terminal end apparatus, a progressive impairment of hearing, grave in its extent and more or less permanent in its degree. Soldiers entering the war with an auditory apparatus intact are more liable to escape injury than those who have been the subject of previous inflammatory process of the middle ear or some measure of impairment or morbidity of the sound-transmitting apparatus. In addition all forms of dry otitis are subject

to a rapid increase in their tissue change under exposure to excessive irritation of loud sounds, the clinical histories of many of the ear patients showing the rapid sequence of degenerative, dry inflammatory conditions of the middle ear following ear injuries at the front. Ruptured tympanic membranes heal without suppuration, and with restoration of function in from five to twenty-one days under proper aseptic treatment, the duration of the impairment being much prolonged by the occurrence of suppuration, the convalescence being considerably shorter than in cases of middle-ear suppuration in civil practice, uncomplicated middle-ear suppuration yielding quickly to dry treatment, probably because the condition is primarily traumatic and not due to some underlying systemic condition. The treatment of rupture of the drum-head and the prevention of complications is effected by the encouragement of spontaneous repair, secured by the prevention of infection, the treatment being aseptic dry treatment, removal of the moisture in the meatus by wiping, insufflation of sterile boric acid powder and plugging of the external canal with sterile absorbent cotton painted with collodion, this treatment being repeated sufficiently often to secure the desired protection against a suppurative process, the treatment of suppurating middle ears and consequent complications being the same as that required in civil practice. In lesions of the auditory nerve the acute cases give the best prognosis, but complete restoration of function cannot be expected, the treatment of these cases being prolonged rest, with general hygienic attention. In cases of nerve lesions of gradual onset, as the result of continued exposure to loud noises, no improvement was to be expected.

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**Apparatus for the Application of Cold Air to the External Canal.**—GRANT (*L'Organe de l'Audition*, Juin et Aout, 1916). In view of the number of cases with sequence of acute or suppurative middle-ear disease examined for military service, the caloric test, by means of the injection of cold and warm water into the external auditory canal, is open to the objection of the possibility of reawakening the activity of a past inflammatory process, and less injury is likely to result by the application of either the galvanic test or, for purpose of control—a dry caloric process, for which purpose the author's instrument serves an excellent means of application. This instrument consists of a tube of metal, of good conductivity copper for instance, in the form of a spiral, with a removable tip to the end of the tube to be inserted into the external auditory canal, permitting removal and sterilization. The cone of tubing is covered with an absorbent gauze saturated with ethyl chloride, the evaporation of which chills the tube and, correspondingly, the air which is passed through it by means of a thermos cautery bulb, the desired degree of chill being attained in from ten to fifteen seconds after the saturation of the gauze. This instrument was first described as a cold-air labyrinth test apparatus in the *Lancet*, in July, 1914, and has achieved value in subsequent tests incident to war conditions.

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**Changing Methods and Advances in the Treatment of Progressive Deafness from Chronic Secretory Otitis Media.**—EMERSON (*American Laryngological, Rhinological and Otological Society, reported in Laryngoscope*, January, 1918). In this paper the author desires to draw atten-

tion to the importance of the consideration of possible remote causes of infection operating systemically to actuate progressive changes in the middle-car sound-transmitting apparatus in distinction from those more immediate exciting causes in the nose and nasal pharynx, basing his communication upon the results of a questionnaire as to the expectation of improvement in such cases from treatment of the nasopharynx, excluding the epipharynx and inflation of the middle ear. To prove that positive improvement in hearing resulted from the cure of remote foci was not an easy problem, as the testimony of the patient, or the aurist, was of no scientific value unless such observations were supported by careful hearing tests, and records covering a term of years, for one was dealing with a chronic disease, subject to acute exacerbations, and varying acuity of hearing. Further, in order that such records should be available for analysis, such observations should extend over a period of from three to five years. From his study of the subject the following conclusions were drawn: "(1) Every case of chronic progressive middle-car deafness has a primary focus; (2) such primary focus is usually constant for the individual; (3) every case showing variable hearing can usually be improved up to their best hearing; (4) Inflation in chronic cases is unscientific and harmful as a routine; (5) nasal obstructions do no harm to the middle ear unless infection is present; (6) foci wherever found are potential factors in the progress of chronic progressive otitis media; (7) no hearing test will forecast the improvement in a given case as long as we have a positive Rinné with variable hearing; (8) whatever the microscopic appearance of the membrana tympani, the cause of the deafness is active for a long time outside the middle ear as a toxemia or low-grade infection subject to acute exacerbations."

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**Acute Suppurating Mastoiditis without Tympanitis: Perisinus Abscess, Phlebitis, Streptococcemia, Operation, Recovery.**—LONG says (*Ann. Otol., Rhinol. and Laryngol.*, June, 1917) that the case here reported by the author illustrates the possibility of extensive infection of the mastoid, with considerable destruction and serious complications, with only a minimum degree of evidence of disturbance in the tympanic cavity, which served as a transitional medium between the point of primary infection and its ultimate exhibition. A girl, aged twelve years, with the history of severe pain in the left ear of five days' duration, accompanied by chills, fever, nausea and vomiting, sleeplessness and delirium, with severe pain and tenderness in the left mastoid region. Temperature, 104.2; pulse, 120; respirations, 36, but without discharge from the external auditory canal, no apparent inflammatory process within the tympanic cavity, and with a membrana tympani moderately reddened, and with the larger bloodvessels injected. An incision of the drum-head liberated no fluid other than blood, and the gauze inserted in the auditory canal and removed the following day was marked only by the dry blood from the incision which had in no way tended to an abatement of the symptoms, except that there was less complaint of pain in the head; the patient was more toxemic, sleepless and delirious. On the ninth day symptoms of meningitis were still more pronounced and the simple mastoid operation was determined upon. The inner table was found carionecrotic, the greater portion being removed by

the curette, exposing small pockets of pus and masses of exudate which completely covered the sinus, and the bone was removed in every direction until healthy dura appeared. The examination of the vein from the knee to the tip of the jugular bulb gave no evidence of thrombus and a long incision gave a free hemorrhage from both ends without clots. This hemorrhage was controlled by packing, with a superposition of moist dressing. On the day following the operation there was no marked improvement, but the tongue was moist, but meningeal irritation had not increased. The laboratory finding of pus from the mastoid showed streptococci. On the next day, there being little change in the condition, a lumbar puncture was made. The spinal fluid was found normal and not under pressure. Under these conditions the treatment consisted in nursing, the necessary surgical dressings, and the patient made a good recovery, being able to leave the hospital twenty-three days after the operation.

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## PATHOLOGY AND BACTERIOLOGY

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**Observations on the Stability of the Erythrocytes of the Ox, Pig and Sheep.**—Though it is customary to use sheep's corpuscles in preparing the usual amboceptor for the Wassermann test, experience has shown that these elements in the Noguchi method are not so stable nor so resistant to human sera as the corpuscles of various other animals. LYON (*Jour. Infect. Dis.*, 1918, xxii, 49) showed that erythrocytes of the ox and pig give even better results than those of the sheep. A working amboceptor was made after five intravenous injections of ox corpuscles into a rabbit and proved to be so satisfactory with the Noguchi method that the sheep system was gradually abandoned and the ox system used exclusively, employing two antigens, alcoholic extract of human heart and cholesterolized extract. Experiments were made by testing the erythrocytes of the pig as well as those of the sheep and ox with a varying number of human sera, 123 in all. In no instance were the sheep cells more resistant than those of the ox or pig. No satisfactory explanation of this fact can be given. There is no explanation nor proof other than the observed fact that human sera contains a natural antisheep amboceptor. Zoologically the sheep and the ox are closely related, and one would expect their corpuscles to behave similarly under the influence of a serum obtained from an animal as zoologically remote as man. On the other hand, the zoologically unrelated ox or pig behave similarly, so far as their erythrocytes are concerned, under the influence of human serum. The well-known case with which the antisheep amboceptor can be prepared appears in part at least to depend on some inherent weakness of the sheep erythro-

cytes. But the fact that they are unstable makes their use in complement-fixation tests with human serum unreliable. Ox erythrocytes seem to have better keeping qualities than the erythrocytes of the pig or sheep.

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**Studies in Immunity against Staphylococcus Pyogenes Aureus.**—The important part played by liver and spleen in ridding the blood stream of infecting organisms was emphasized years ago by Wyssokowitseh and Werigo. Recently, BARTLETT and OZAKI contributed a very enlightening paper (*Jour. Med. Research*, 1917, xxxv, 465) on the same subject, showing the relationship of phagocytosis of bacteria by these organs and by the lungs. In continuation of this study, ITO (*Jour. Med. Research*, 1917, xxxvii, 189), of the same laboratory, has considered the fate of living staphylococci when introduced into the jugular vein of actively immunized dogs and of killed bacteria introduced intravenously into normal dogs. Positive agglutination in dilutions of 6000 to 10,000 was used as the index of immunity. The animals were killed at periods varying from ten minutes to ninety-six hours after the last injection. Bacteria could not be found in blood smears later than one hour after injection, and they never reappeared. No mention is made of cultures. In the dog killed ten minutes after injection very few cocci were seen in the blood smears, and these were within the leukocytes. The bacteria had disappeared from the tissues within twenty-four hours. The author's conclusions are as follows. "(1) Bacteria introduced into actively immunized dogs disappear sooner than in normal dogs, and never were found in any part of the body. (2) Bacteria that accumulate in the lungs in the earlier stage are transported to other organs, but they are not found in the spleen in large numbers, while they are more numerous in the liver; (3) in the several organs it appears that both fixed and wandering cells have the ability to engulf, as well as to digest, bacteria throughout all stages; (4) as to the fate of the killed bacteria introduced into normal dogs, they are destroyed somewhat more quickly than the living bacteria introduced into immunized dogs and they provoke no changes evident histologically in the tissues." OZAKI (*Jour. Med. Research*, 1917, xxxvii, 247), in order to study the phagocytic properties of fixed tissue cells, perfused the excised spleen of a dog with Locke's solution for some hours and then injected into the organ a culture of *Staphylococcus aureus*, not through the blood channels but directly into the pulp. As a control the same organisms were injected deeply into the spleen *in situ* in the living animal. "Wandering cells, as well as fixed tissue cells, show, if at all, but slight necrobiotic changes, and their function is well carried out in so far as bacterial ingestion is concerned." In the spleen of the living animal, as well as that kept alive by means of Locke's solution, the bacteria injected into the parenchyma are principally ingested by splenic cells, polymorphonuclear leukocytes and to some extent also by living endothelial cells and endothelial leukocytes. In the living animal the grade of phagocytosis by the polymorphonuclear leukocytes found in the spleen is on an average far more pronounced than that by splenic cells. A similar relation is also observed, although somewhat less marked, within the spleen tissue kept alive by means of Locke's solution, provided that these cells do not undergo any, even slight, necrobiosis.

**A Contribution to the Study of War Nephritis.**—Since the beginning of the war a number of papers have appeared dealing with the occurrence of nephritis among soldiers on active duty. The various observers have insisted upon the occurrence of a disease among soldiers which bears no relation to any previous kidney infection or systemic illness as may be found in civil life. It is obvious that with the aggregation of such large numbers of men there will be found sporadic cases of recurrent nephritis which escaped the attention of the recruiting officers. Besides this, with the appearance of active infections like typhoid, dysentery, pneumonia or those of the heart, Bright's disease in different grades of severity are met with in the frequency seen in civil hospitals. Over and above this, however, there has appeared a type of nephritis bearing no relation to a previous illness nor appearing as a complication of another disease. This form of nephritis has occurred among the men on active duty in the trenches, while the soldiers who have not been on the firing line and the civilian population in the near vicinity are relatively or completely immune to the affection. DUNN and MCNEE (*British Med. Jour.*, 1917, ii, 745) have lent particular attention to the study of nephritis and have collected many cases among the British Army at the front. For obvious reasons they are unable to state the exact number of men examined and the incidence of the disease. They point out that they were unable to associate the varying incidence in different companies with the climatic conditions nor with the conditions under which the men were living. The disease may be very insidious in its onset, the most common clinical manifestation being dyspnea. Next in frequency they found edema, pain in head, epigastrium or back, sore throat and hoarseness, in the order named. The edema appeared as a puffiness about the face or extremities. Fever was present in only a few cases and uremia was rarely seen. The urine contained large quantities of albumin, but showed little diminution in quantity. Casts were always present in varying numbers. The bacteriological examination of the urine showed the presence of bacteria in more than half of the cases examined, the streptococci being the commonest organisms found. The authors had an opportunity of studying the tissues from 35 cases of true war nephritis, in which the characteristic lesion was of the glomerular type. The glomeruli were cellular, showing some leukocytes and lymphocytes, but never showing blood thrombi. Granular occlusions of the glomerular loops were observed in a few cases. A true inflammatory exudate was wanting and the interstitial tissue between the tubules showed but little reaction. Various grades of degeneration of the tubular epithelium was observed, but it was never the outstanding change. The medulla of the kidney showed an edema and hyaline change of the connective tissue. The authors also observed peculiar changes in the lung. These consisted of an interstitial edema, without an associated pneumonic process. The lung lesions, they claim, are suggestive of a respiratory irritant, not unlike that obtained in gas poisoning. In the brain, minute hemorrhages about small vessels were also seen. The authors state there is no evidence that the nephritis is due to bacterial infection. They suggested a relation between the pulmonary lesion and the changes occurring in the kidney.

**Experimental Immunity to Cancer.**—BULLOCH and ROHDENBERG (*Jour. Cancer Research*, 1917, ii, 455 and 465) have contributed some interesting experiments on the relation of induced cancer immunity to tissue growth and tissue regeneration and on the possibilities of an immune influence by splenectomy. Immune substances seem to arise from living cells, whether from the products of metabolism of their growth or of their death or of growth followed by death. The growth power of embryo cartilage is greater than that of embryo skin, yet when the former was injected into one series of rats, and the latter into another, and both series shortly inoculated with Flexner-Jobling carcinoma, the percentage of immunity to this was as 19 to 30, *i. e.*, in favor of those rats injected with embryo skin. The authors suggest that superiority of the skin in cell elements and in active proliferation may account for its greater power for stimulating immunity. To determine the immunizing action of degenerative metabolites, large doses of embryo skin were injected for purposes of immunization and degenerative changes occurring early, much necrotic material resulted. Later these rats were injected with Flexner-Jobling carcinoma, and this material was removed and studied in various stages of degeneration. Fully two-thirds of it showed complete degeneration before the fifth day, but immunity had not arisen in all. "It is impossible to determine by the local reaction of the animal toward the immunizing agent, or by the condition of that agent, whether an animal will be susceptible or immune to a transplantable tumor." These workers then wished to investigate whether increasing absorption of products of cell-degeneration might not favor immunity, and they used the Flexner-Jobling carcinoma, which does not produce concomitant immunity nor that which arises when a tumor grows for a period and then recedes. Degenerative products were obtained by transplanting into the shoulder of a rat the tumor mass which for eighteen days had been in its side. Eleven days later the same tumor strain was injected, but the degree of immunity was about the same in these rats as in the controls. In another experiment it was shown that an initial small dose gives more immunity than a large one. The authors conclude that "induced immunity to transplanted cancer is not solely due to growth or the metabolites of growth of the immunizing agent, nor is it due to death and the degenerative metabolites of the injected material." The experiments involving splenectomy were performed because of the alleged influence of lymphocytes in immunity to transplanted tumors. Using a tumor which is spontaneously absorbed, they showed that "splenectomy does not influence the persistence of immunity in animals." Neither did removal of spleen affect the regression of a previously injected tumor producing concomitant immunity. Removal of the spleen or testes had no effect upon the immunity induced in adult mice by embryo emulsion. Further, splenectomy neither increased the percentage of takes nor favored the growth of spontaneous tumor grafts.



## HYGIENE AND PUBLIC HEALTH

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**Drinking-water on Interstate Carriers.**—COBB, WILLIAMS and SETTON (*Public Health Reports*, October 13, 1916, xxxi, No. 41) state that the frequent occurrence of typhoid fever among sailors on the great lakes first caused investigators to make a study of this problem. In 1913 the interstate quarantine regulations were so amended as to put the control of drinking-water supplies aboard interstate common carriers under the supervision of the U. S. Public Health Service. The regulations which govern the water supplies of interstate common carriers are briefly as follows:

"Sec. 13. Water provided by common carriers on cars, vessels or vehicles operated in interstate traffic for the use of passengers shall be furnished under the following conditions: (a) Water shall be certified by the interstate sanitary officers or the State or other authorities within whose jurisdiction it is obtained. (b) The ice shall be produced under proper conditions if it is to be used in contact with the water. (c) Water containers shall be cleansed at least once a week.

"Sec. 14. Interstate carriers shall not furnish their crews with contaminated water nor shall they maintain any receptacle, tank or article which may contain impurities which may affect said water.

"Sec. 15. No person, firm or corporation shall furnish water for drinking or cooking purposes to any vessel in any harbor of the United States which has been taken from any harbor or place where it may have been contaminated.

"Sec. 16. Common carriers shall not furnish for the use of passengers in interstate traffic any water taken from a lake or stream over which the vessel is being navigated unless this water is certified by the U. S. Public Health Service or State or municipal authorities as conforming to the bacteriological standard for drinking-water promulgated by the Secretary of the Treasury."

To carry out these regulations the continental United States was divided into 12 interstate sanitary districts, one of which is the district of the Great Lakes with headquarters and laboratory at Chicago. There are two methods generally used to obtain water on lake vessels, by pumping or by gravity through a sea-cock, consisting of a flanged valve bolted directly to the shell of the vessel in the hull, and secondly, by filling the drinking-water tanks through a hose from a hydrant on shore. These tanks are usually well aft and are constructed of heavy galvanized iron or sheet steel, very few of them being lined. Sometimes

the construction is faulty, permitting contamination from various sources. On most vessels there are two and sometimes three systems of water supply: the drinking-water which supplies drinking fountains, kitchens and wash basins, the "sanitary" system which furnishes the water for flushing toilets, and the fire system which is also used for washing down decks and other purposes. The drinking-water system is the only one under consideration. The water is distributed either by gravity from a storage tank located on an upper deck or by a special distributing pump which maintains a constant pressure in the system. Investigations of these systems of taking in and distributing water have revealed the fact that there are many opportunities for contaminating the drinking-water thus obtained. Among these are contamination of the sea-cock or suction pipe while in polluted water, faulty placing of valves, failure to close the valves, contamination from the sewage system of the ship and accidental or intentional taking of supplies in polluted water. Because of the poor quality of the water obtained, it has been necessary for each vessel to install some form of water purification apparatus. The most common form of treatment is the use of rapid sand filters which this investigation proved to be of extremely low bacterial efficiency. Other vessels used the ultra-violet ray sterilization, eleven of the vessels having the pressure type of apparatus and two the gravity type. The objections to this method were several: the voltage was not high enough to obtain a sufficient intensity of the ultra-violet rays, there was often a sudden fluctuation of voltage, causing the lamps to go out; and the efficiency of the ultra-violet lamps was lowered because the water exposed to the rays was not clear. On five vessels, the water supply was treated with calcium hypochlorite. The efficiency of this depends on the proper proportion being added to the tanks, and this proportioning was not carefully done. Another method of chlorine disinfection was by using an apparatus for treating the water with liquid chlorine. This machine is rather complicated and as the chlorine solution is constantly becoming diluted, it requires chemical tests on the treated water to know just when this solution becomes too weak to be efficient. The apparatus which treated the drinking-water by heating with a steam jet, while it produced good results under careful management, was liable to be mishandled. A total of 961 samples were collected and examined from 74 passenger steamers and 33 freight vessels. The results from these examinations showed that the methods of purification are inefficient, only 38.9 per cent. of the samples treated in rapid sand filters conforming to the standard and only 31 per cent. of the samples treated by the ultra-violet ray method. Of the samples treated by the heat method, 69.2 per cent. conformed, of those disinfected with hypochlorite, 60 per cent. conformed and of those treated with the liquid chlorine, 84.2 per cent. conformed. A study of results according to the route of the vessels showed that those travelling in polluted waters and docking in contaminated harbors showed that the samples from such vessels had a higher bacterial count than from vessels running in better water. In concluding, the authors recommend as the ideal apparatus for water purification, the still. It requires but little care, and it is not necessary to pay attention to the place of taking the supply of water. They have demonstrated that heating by steam jet and exposure to ultra-violet rays are capable of producing a water conform-

ing to the standard if everything about the apparatus is in good order and it is carefully operated, but, as experience has shown that these conditions usually do not exist, purification by means of a still is far more satisfactory.

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**The Grading of Milk in Small Communities.**—WILLIAMS (*Am. Jour. Public Health*, October, 1916, vol. vi, No. 10) states that prior to the enactment of the Sanitary Code in New York State, comparatively few small communities had progressed very much in grading the milk supply. Although it has decided limitations, the grading of a milk supply is by far the most satisfactory method of improving the sanitary quality of the milk supply of a community. For a number of years the 3 first-class cities in the State of New York have kept the milk supply under a satisfactory system of supervision, but in the 7 second-class cities only 1 had any system of grading the milk supply and of the 47 smaller cities of the State, that is, having a population of less than 50,000, only 2 made any definite attempt to grade their milk supply prior to the adoption of the Sanitary Code. The adoption of this code has caused an improvement in the milk supply throughout the State of New York. The articles of this code charge every municipality with the duty of supervising its milk supply through its health officer and his agents. They consist in the inspection and scoring of dairies and the classification of the milk into grades, according to the dairy score and bacteriological count. The tuberculin test and bacteriological count are required for certified and grade A milk and physical examination, excluding tuberculous cattle for grade B milk. Previous to the adoption of the Sanitary Code, the village of Saranac Lake worked out quite an effective system of grading its milk supply, the three grades adopted being very similar to those adopted later by the State Department of Health. The city of Ithaca started in 1909 to improve its milk supply. The milk was graded on the basis of bacteriological counts and on the standard score card. A physical examination of all the dairy cattle supplying milk to the city was required, and the dairy scores, giving the bacteriological count and grading for the month were published. In other small communities some provisions have been made for grading the milk supply and an improvement of the scores and bacteriological counts has been noted but this work was limited. However, since the adoption of the State Milk Code many incorporated villages and small cities are now actively carrying on campaigns for grading their milk under the direction of the health officer and an effort is being made to explain to local dealers the meaning of the regulations which require the grading of milk. Thus, at the completion of the first year of work after the adoption of the milk code, a great improvement is shown in the milk supply of small communities throughout the State.

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**The Prophylactic and Therapeutic Properties of the Antitoxin for *Bacillus Welchii*.**—BULL (*Jour. Exp. Med.*, October, 1917) reports that the results of his experiments with the preventive and therapeutic applications of the antitoxin are highly suggestive. They derive significance from the fact that *Bacillus welchii* infections in guinea-pigs and other susceptible animals are comparable with infections with this organism in man. The experimental infections in the guinea-pig differ,

however, from the natural infection in man in two important points: (1) man possesses a higher natural resistance to infection; (2) the guinea-pigs were infected with fresh virulent cultures, while man must, in the great majority of instances, derive infection from spores. Moreover, the protected guinea-pigs were given many lethal doses of the living cultures. Such massive inoculations do not occur in man. It may therefore be safely predicted that man will not develop the infection as long as his body fluids and tissues contain adequate quantities of the antitoxin. The possibilities of this passive serum protection has natural limits of time, depending upon the rapidity of elimination of the foreign serum. The experimental data presented by Dr. Bull, which agree with the experience with antidipltheritic and antitetanic antitoxins, indicate that, in all probability, a passive immunity to *Bacillus welchii* infection of at least two weeks' duration can be conferred upon man by a single injection of the antitoxin. This immunity will be sufficient in the majority of instances, since only sporadic cases of *Bacillus welchii* infection arise later than the tenth day after injury, and the greater number occurs within forty-eight hours of that time. In the light of the results obtained by Bull in treating the infection in guinea-pigs, he regards it as reasonable to hope that the antitoxin will be of value also as a therapeutic agent. The indications are that early infectious cases can be readily arrested and the more advanced and severe ones ameliorated, if not wholly checked, so that surgical interference may be resorted to with greater probability of effectiveness. The antitoxin in man should be administered intravenously and probably locally about the wound as well.

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**A Graphical Study of the Epidemiology of Poliomyelitis.** HULL. (*Am. Jour. Pub. Health*, October, 1917, vii, No. 10, p. 813) concludes from his studies that poliomyelitis follows the main routes of travel, indicating that it is probably carried by human agencies. It spreads in waves over the country, the crest progressing steadily away from the focus. This suggests that in severe outbreaks practically everyone is exposed, and, after all the susceptibles have been stricken, the epidemic subsides. The seasonal prevalence is quite marked, the large majority of cases occurring between the first of June and the last of November. In the southern hemisphere the seasons are reversed, the epidemics occurring between the first of December and the last of May. Out of 34 epidemics occurring during the last seventy-five years, 76 per cent. began in months of deficient rainfall and in 29 per cent. of them the dry weather lasted clear through. Twenty-four per cent. of the epidemics began in excess months, and in none did the wet weather continue clear through. In 18 epidemics with a total of 13,365 cases practically 90 per cent. of the cases occurred during deficiency months. The dryer the weather, in general, the greater has been the number of cases.

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